# Stroke Prevention in AF

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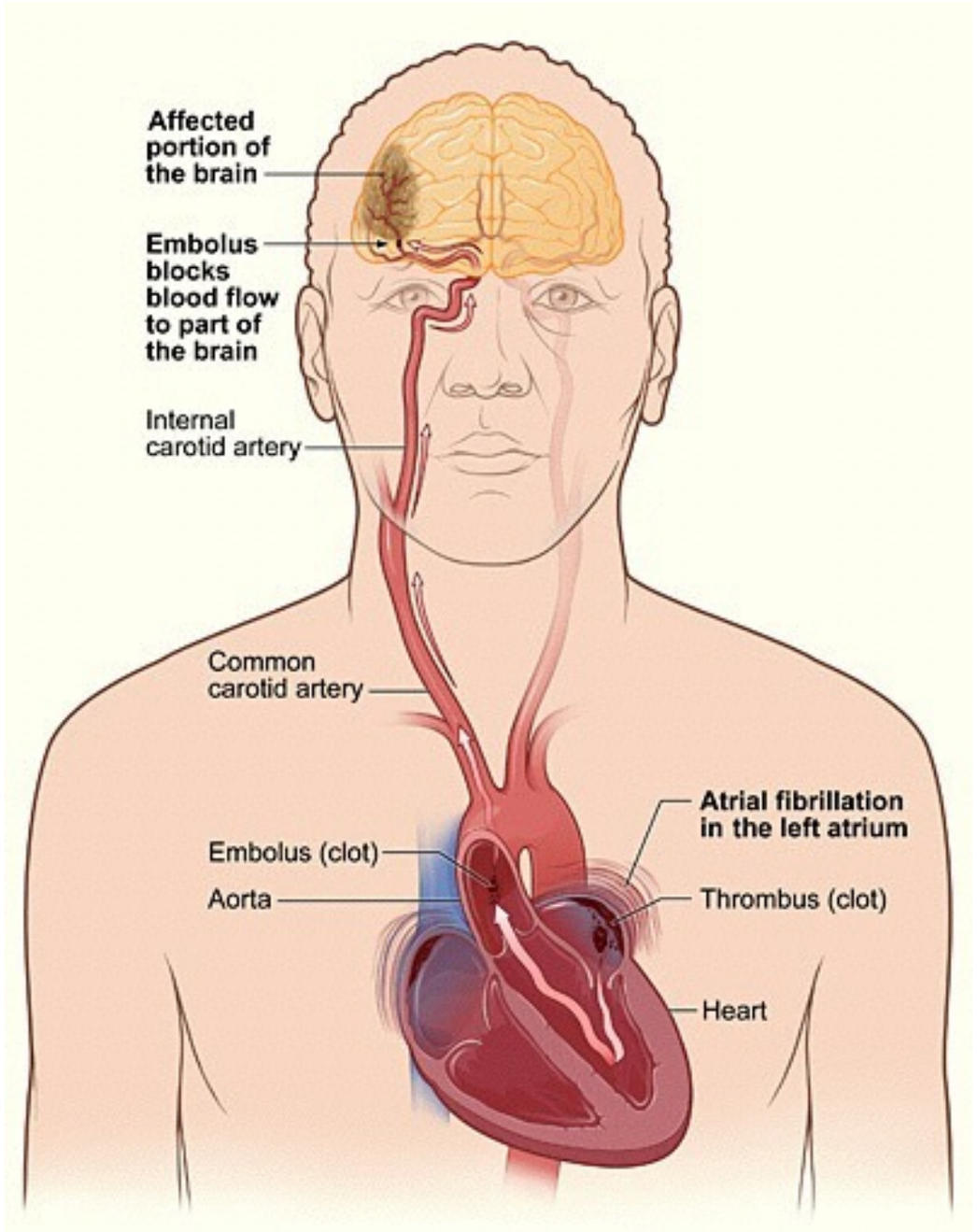
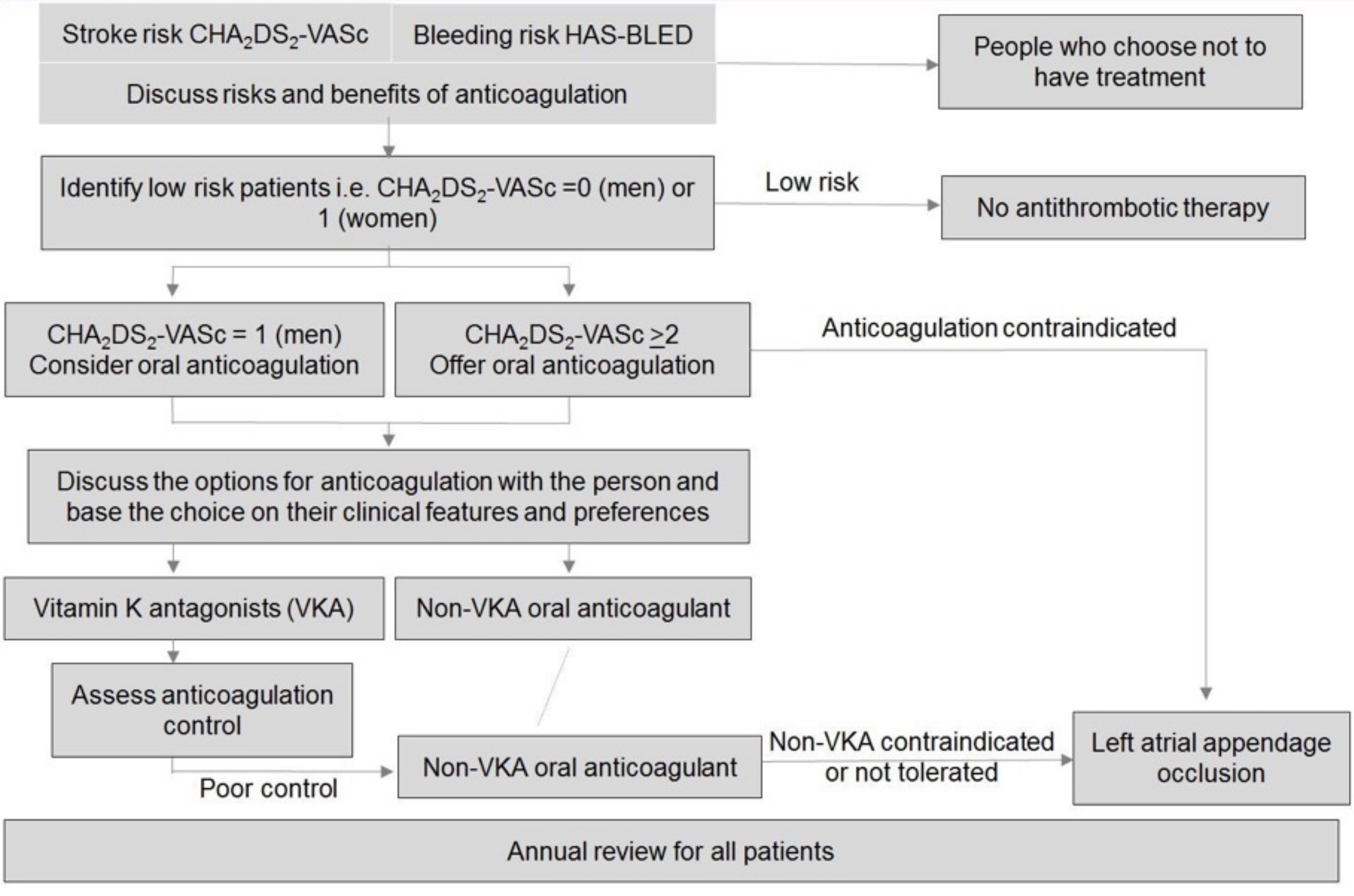
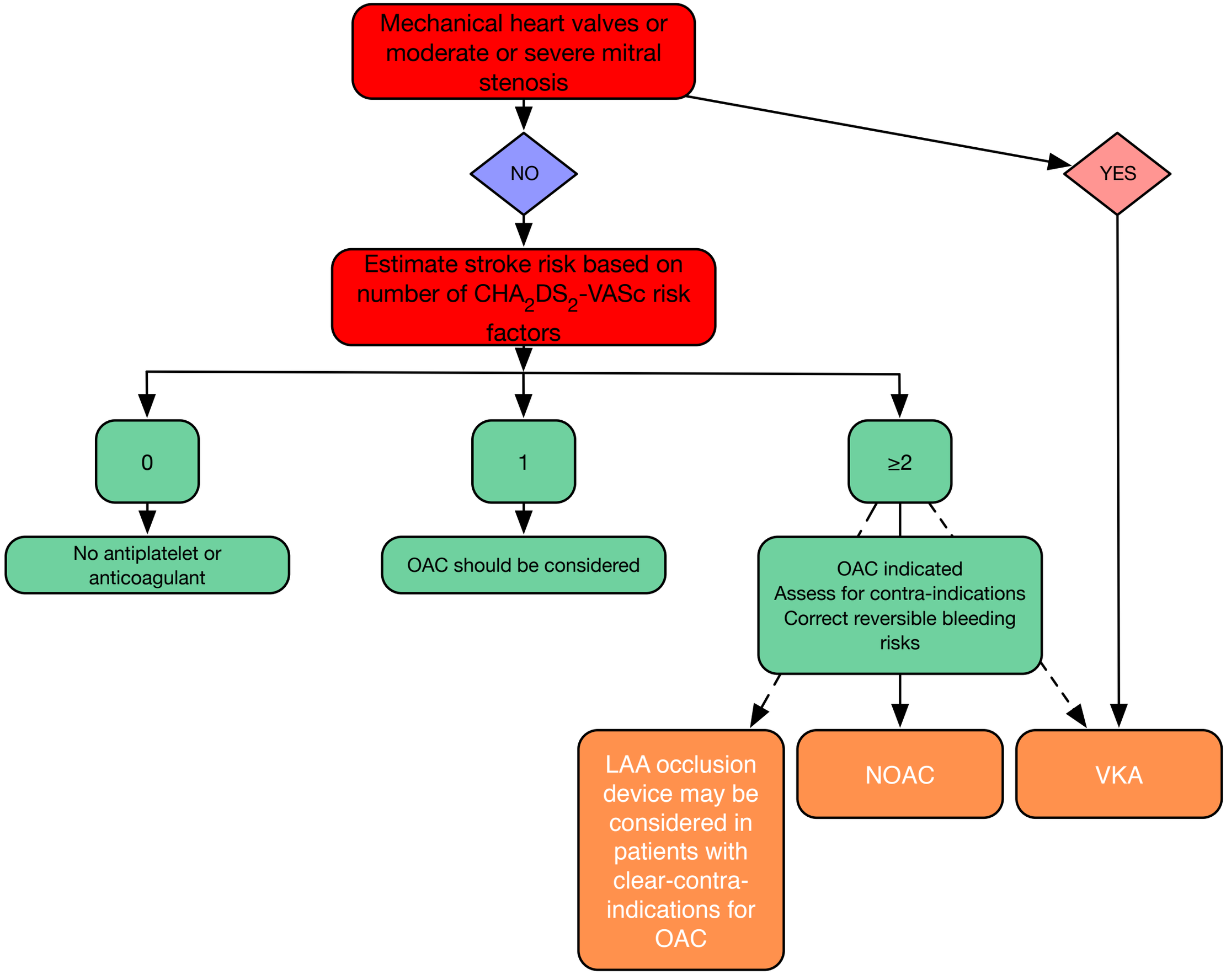
# Stroke and AF



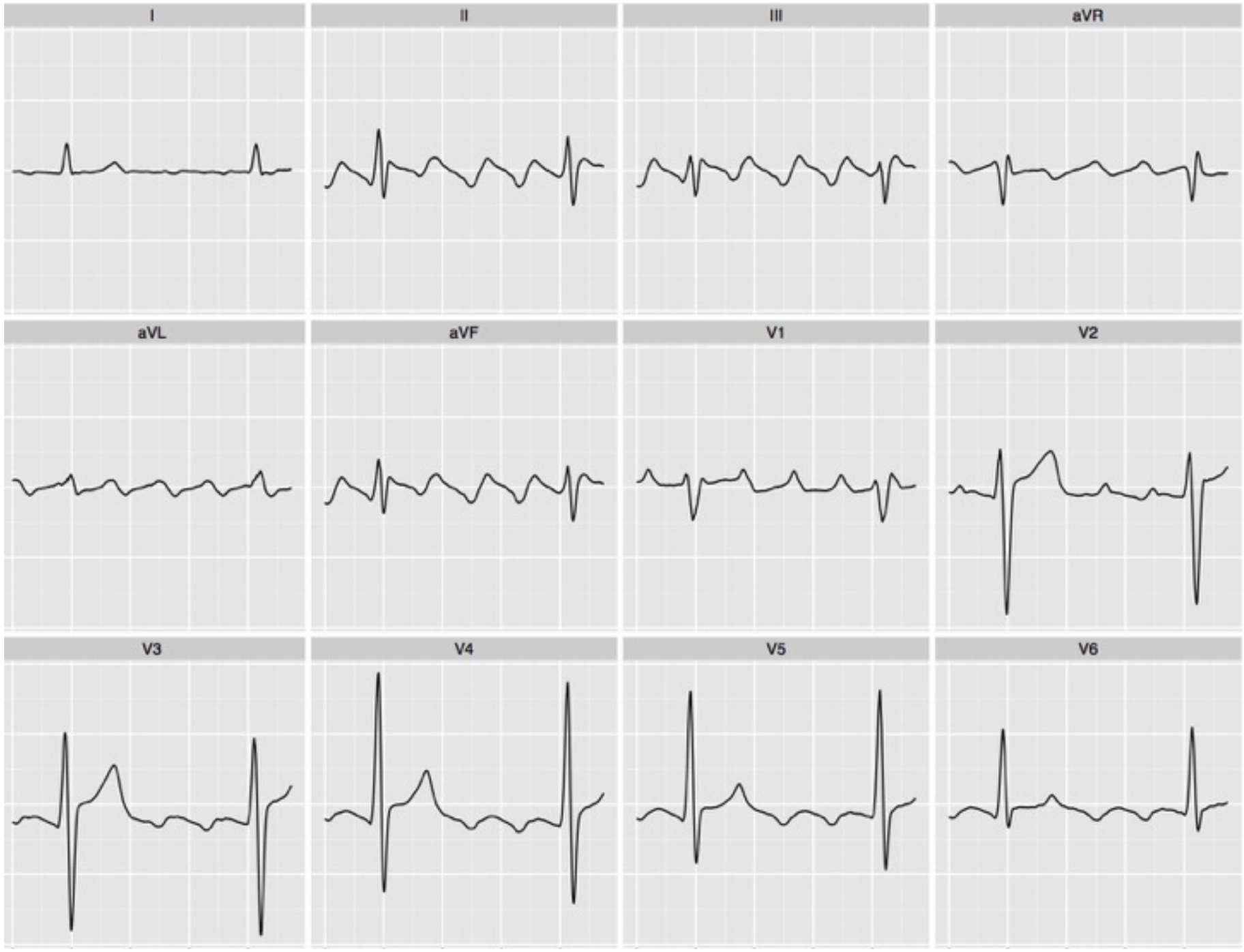
# NICE algorithm for stroke prevention in people with non-valvular AF[8]




8. NICE 2014 AF CG180. Full guideline. Available at: https://www.nice.org.uk/guidance/cg180/evidence/atrial-fibrillation-update-full-guideline-243739981. Last accessed: March 2016


Mechanical heart valves or moderate or severe mitral stenosis
NO
YES
Estimate stroke risk based on number of $CHA_2DS_2$-VASc risk factors
0
1
≥2
No antiplatelet or anticoagulant
OAC should be considered
OAC indicated
Assess for contra-indications
Correct reversible bleeding risks
LAA occlusion device may be considered in patients with clear-contra-indications for OAC
NOAC
VKA

# Flutter



# Using $CHA_2DS_2VASc$ to determine need for anticoagulation[1]

- **NICE guidelines (2014)**
- **Do $CHA_2DS_2VASc$ risk assessment** for all patients:
  - Paroxysmal AF
  - Persistent AF
  - Permanent AF
  - Atrial flutter
  - Risk of recurrence after cardioversion back to sinus rhythm
- If **$CHA_2DS_2VASc \geq 2$ offer** anticoagulation
- If **$CHA_2DS_2VASc = 1$ consider** anticoagulation taking bleeding risk into account



1. NICE 2014 AF CG180. http://www.nice.org.uk/guidance/cg180. Last accessed: February 2016

# The 2014 NICE guideline states to use the $CHA_2DS_2$-VASc stroke risk score instead of the $CHADS_2$ score[2]

| $CHADS_2$ Risk | Score |
|---|---|
| Congestive Heart Failure (CHF) | 1 |
| Hypertension | 1 |
| Age >75 | 1 |
| Diabetes | 1 |
| Stroke or TIA | 2 |

| $CHA_2DS_2$–VASc Risk | Score |
|---|---|
| CHF or LVEF ≤40% | 1 |
| Hypertension | 1 |
| Age ≥75 | 2 |
| Diabetes | 1 |
| Stroke/TIA/ Thromboembolism | 2 |
| Vascular Disease | 1 |
| Age 65–74 | 1 |
| Female | 1 |

LVEF = Left ventricular ejection fraction



2. Camm, A.J. *et al*; *European Heart Journal* (2012) 33, 2719-2747

# Annual stroke risk with the $CHADS_2$ and $CHA_2DS_2$-VASc stroke risk score

**$CHA_2DS_2$-VASc Annual Stroke Risk[5]**

| Score | Stroke risk % |
|---|---|
| 0 | 0 |
| 1 | 1.3 |
| 2 | 2.2 |
| 3 | 3.2 |
| 4 | 4.0 |
| 5 | 6.7 |
| 6 | 9.8 |
| 7 | 9.6 |
| 8 | 12.5 |
| 9 | 15.2 |

4. Prevention of Cardiovascular Morbidity Associated with Atrial Fibrillation CME/CE, Gregory Y.H. Lip, MD, FRCP. Available at: http://www.medscape.org/viewarticle/708955_4. Last accessed: February 2016
5. Chopra, H.K. 2015. *Cardiological Society of India Cardiology Update 2014*. New Delhi: Jaypee Brothers Medical Publishers Ltd.

# HAS-BLED score to assess a patients' individual bleeding risk

**OAC benefits outweigh bleeding risk for most people[1]**

For people with an increased risk of bleeding, the benefit of anticoagulation may not always outweigh the bleeding risk, and careful monitoring of bleeding risk is important[1]

**The HAS-BLED score can change by controlling and monitoring[1]:**

- Uncontrolled hypertension
- Poor control of INR ('labile INRs')
- Concurrent medication, e.g. concomitant use of aspirin or an NSAID
- Harmful alcohol consumption

| HAS-BLED score to assess bleeding risk[6] | | |
|---|---|---|
| **Letter** | **Clinical characteristic** | **Points awarded** |
| **H** | Hypertension | 1 |
| **A** | Abnormal renal and liver function (1 point each) | 1 or 2 |
| **S** | Stroke | 1 |
| **B** | Bleeding | 1 |
| **L** | Labile INRs | 1 |
| **E** | Elderly (e.g. age>65 years) | 1 |
| **D** | Drugs or alcohol (1 point each) | 1 or 2 |
| | | Maximum 9 points |

1. NICE 2014 AF CG180. http://www.nice.org.uk/guidance/cg180. Last accessed: February 2016

6. MD Calc. HAS-BLED Score for Major Bleeding Risk http://www.mdcalc.com/has-bled-score-for-major-bleeding-risk/. Last accessed: February 2016

HAS-BLED Scoring for Risk of Major Bleeding with Oral Anticoagulation.

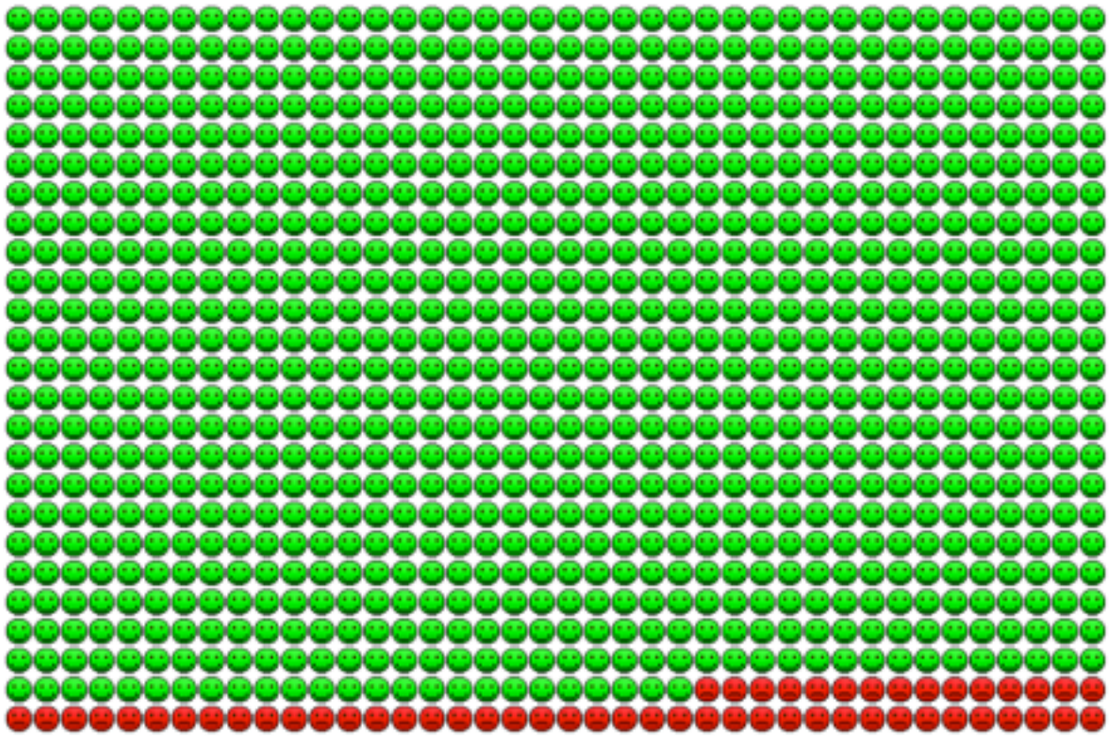
| Category | Score |
|---|---|
| **H**ypertension[1] | 1 |
| **A**bnormal renal[2] and liver function[3] (1 point each) | 1 or 2 |
| **S**troke | 2 |
| **B**leeding[4] | 1 |
| **L**abile INRs[5] | 1 |
| **E**lderley[6] | 1 |
| **D**rugs[7] or alcohol[8] (1 point each) | 1 |

1. Systolic BP >160 mmHg
2. Chronic dialysis, transplantation, Creat>200 µmol/l
3. Bilirubin >2 x normal and AST/ALT >3 x normal
4. Previous bleeding history and/or predisposition to bleeding
5. Time in therapeutic range <60%
6. Age >65 years
7. Concomitant use of drugs such as aspirin and NSAIDs
8. Alcohol consumption >8 u/week

HAS-BLED Score and Annual Risk of Major Bleed.

| Cumulative HAS-BLED Score | Risk of Major Bleed, % |
|---|---|
| 0 | 1.13 |
| 1 | 1.02 |
| 2 | 1.88 |
| 3 | 3.72 |
| 4 | 8.70 |
| 5 | 12.5 |

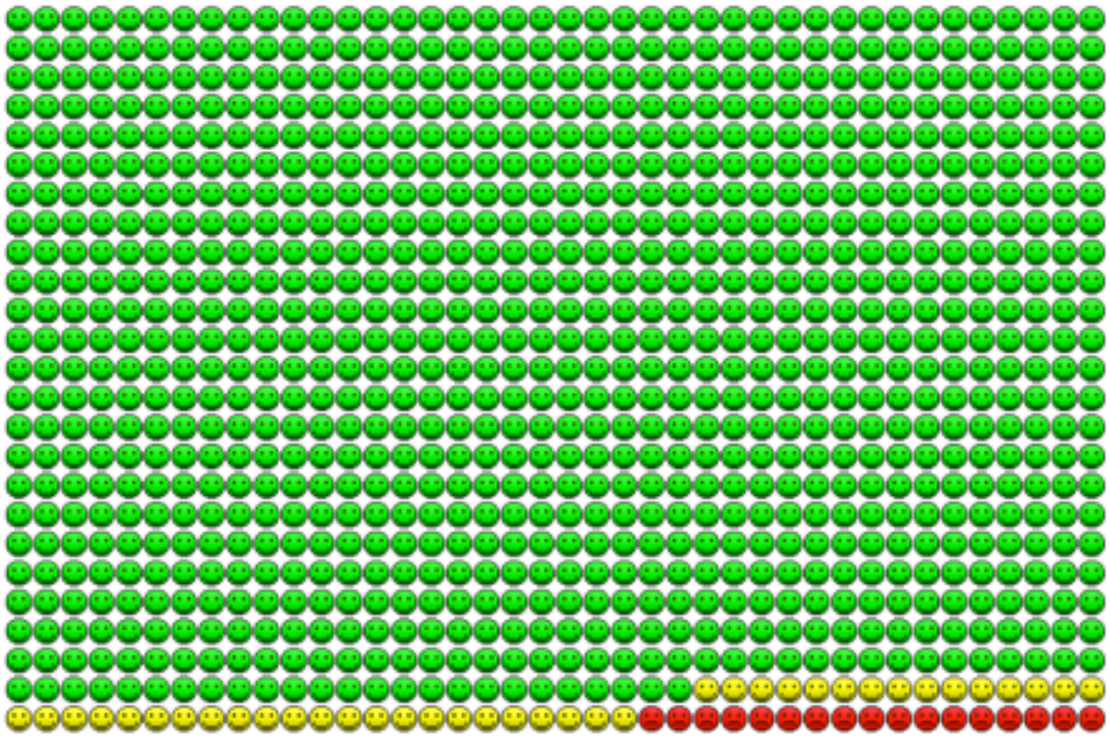
## No treatment: $CHA_2DS_2$-VASc score 4



If 1000 people with AF and a $CHA_2DS_2$-VASc score of 4 take no anticoagulant, over 1 year on average:

- 945 people will not have an AF-related stroke (the green faces)
- 55 people will have an AF-related stroke (the red faces).

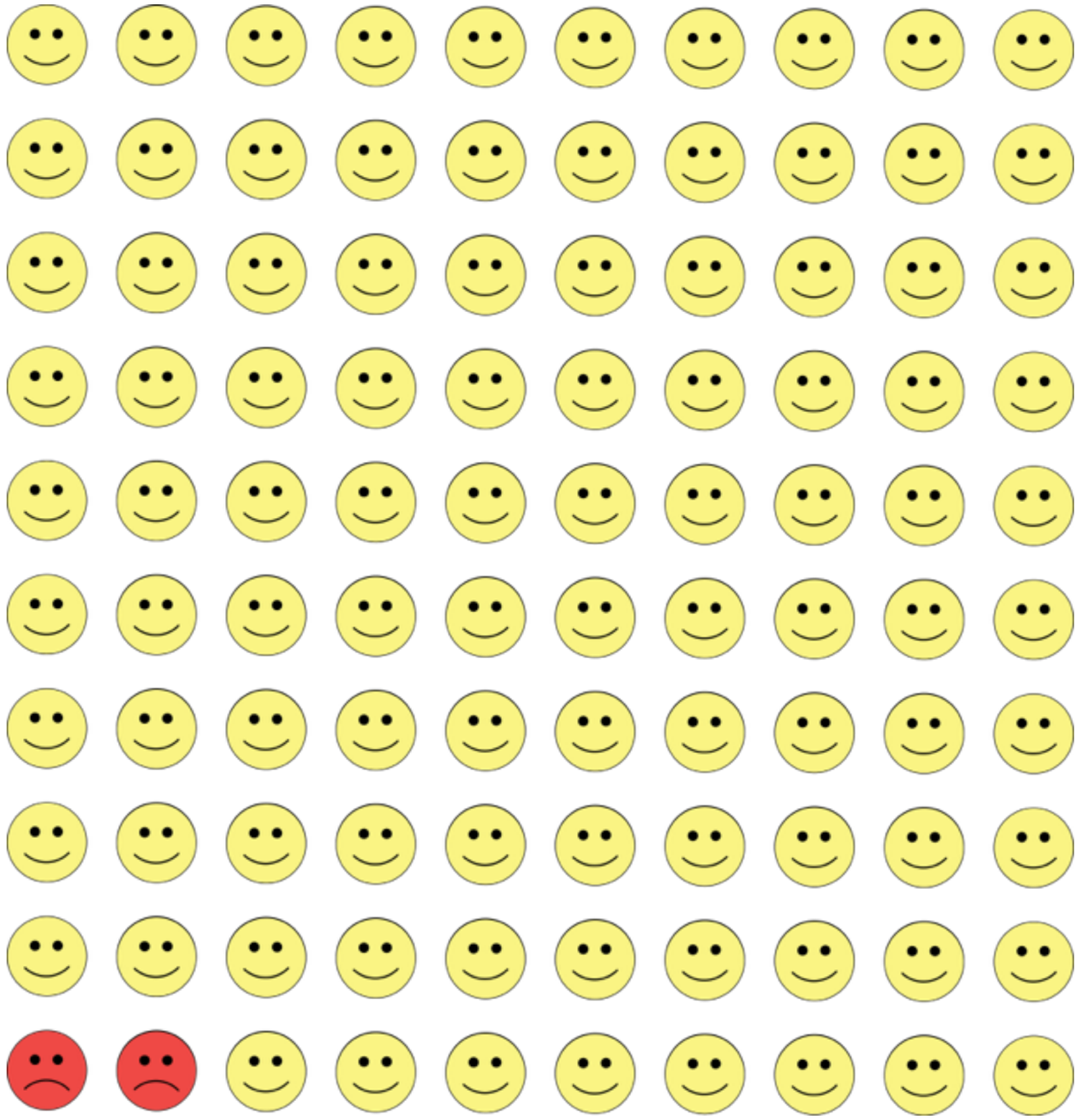
## Anticoagulant: $CHA_2DS_2$-VASc score 4



**If all 1000 people take an anticoagulant**, over 1 year on average:

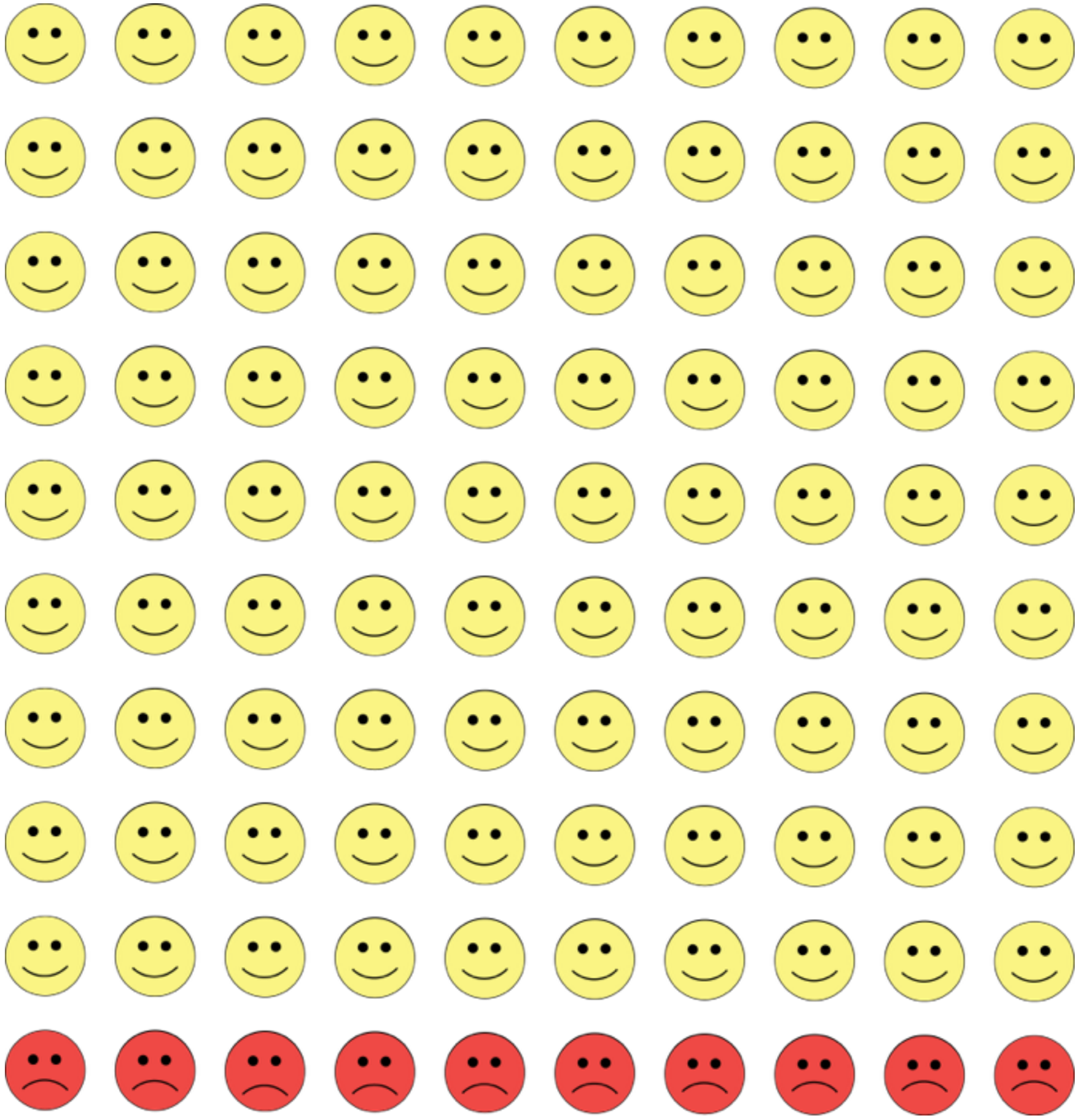
- 945 people will not have an AF-related stroke (the green faces), but would not have done anyway
- 38 people will be saved from having an AF-related stroke (the yellow faces)
- 17 people will still have an AF-related stroke (the red faces).

Score=2
Risk=2.2%y/r

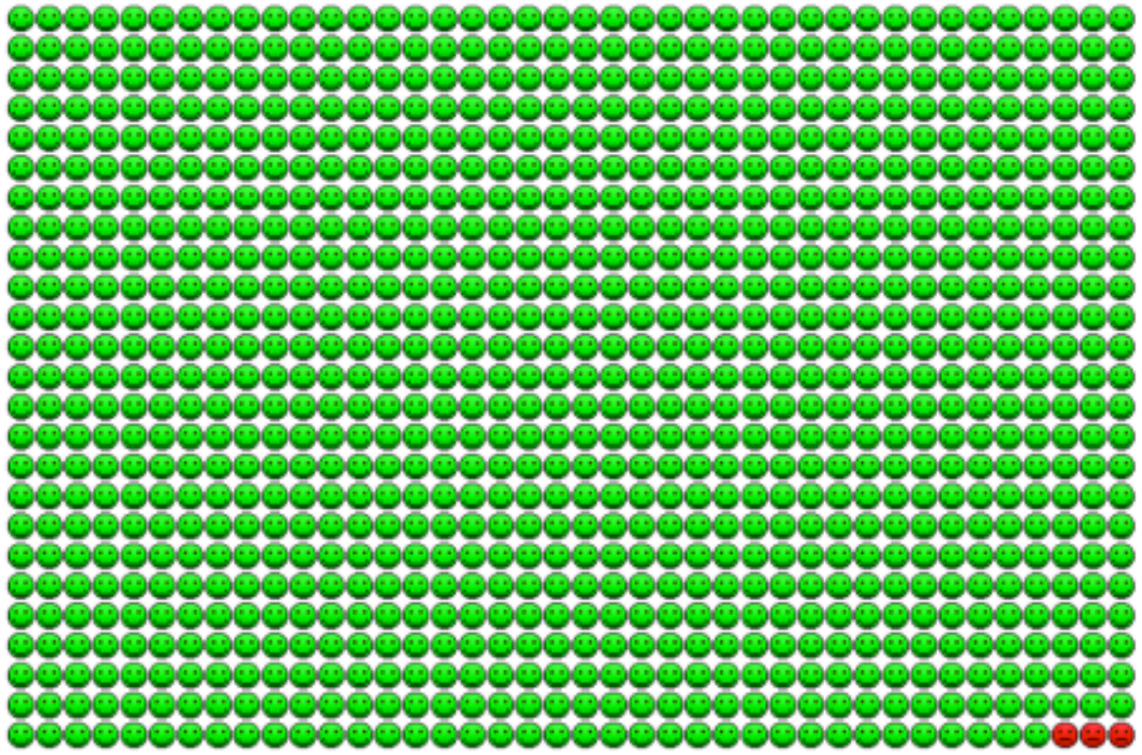


Score=6

Risk
9.8%/yr



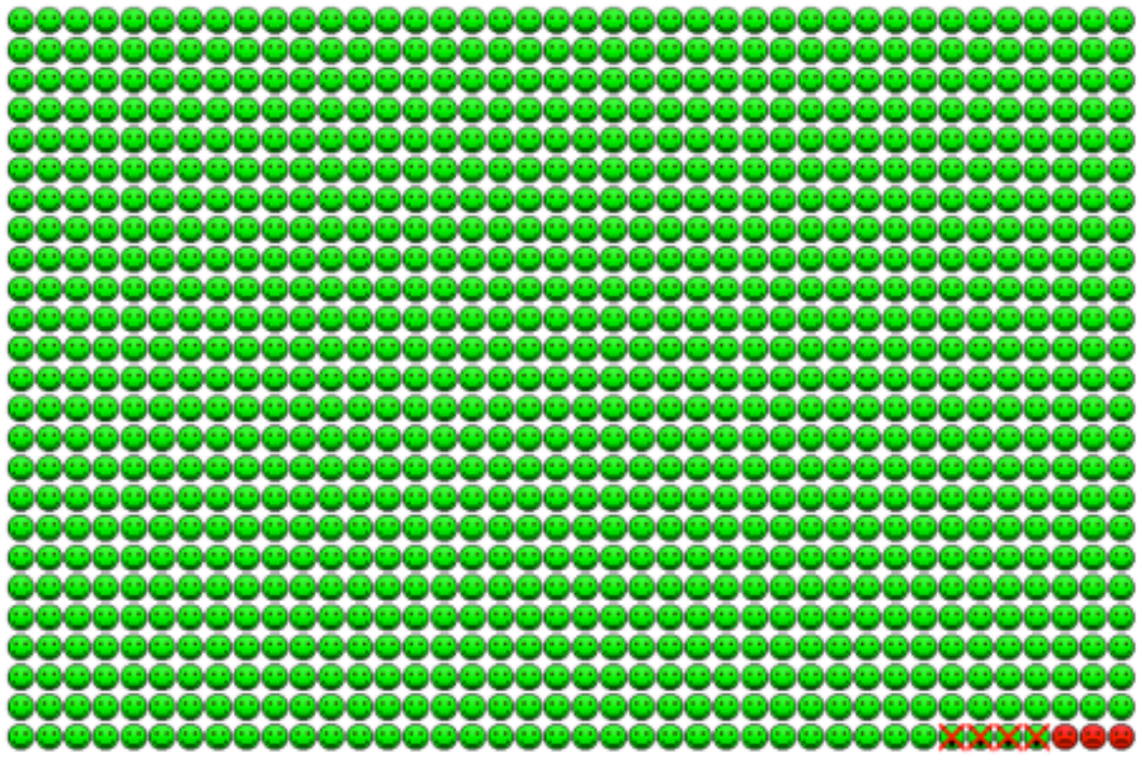
## No treatment: HAS-BLED score 1



If 1000 people with AF and a HAS-BLED score of 1 take no anticoagulant, over 1 year on average:

- 997 people will not have a major bleed (the green faces)
- 3 people will have a major bleed (the red faces).

## Anticoagulant: HAS-BLED score 1



**If all 1000 people take an anticoagulant**, over 1 year on average:

- 993 people will not have a major bleed (the green faces)
- 3 people will have a major bleed (the red faces), just as they would have done anyway
- An extra 4 people will have a major bleed (the green faces with the red cross).

# Reassessing Stroke Risk

- For people without anticoagulation
- Review stroke risk at 65
- Or if they develop any of the following at any age:
  - Diabetes/HTN
  - Heart failure
  - Peripheral arterial disease
  - Coronary heart disease
  - CVA/TIA or systemic thromboembolism

# Anticoagulation NICE 2014

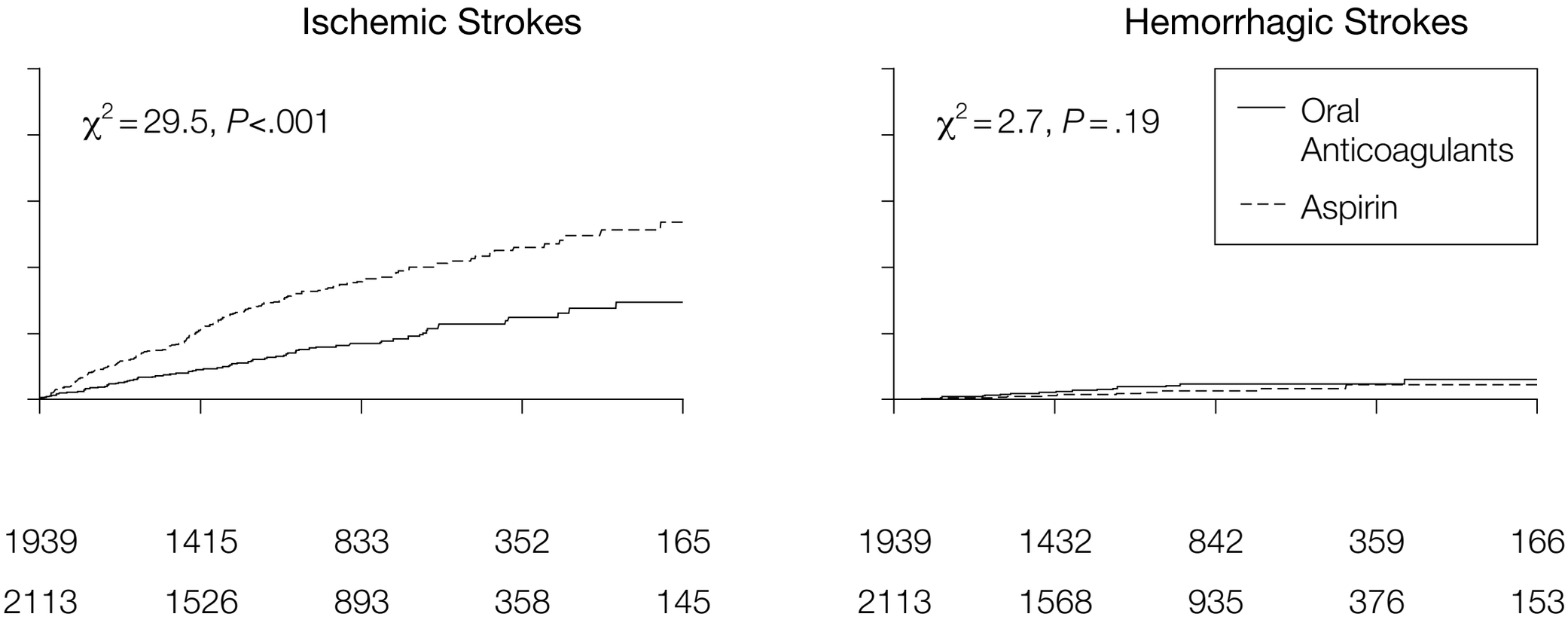
- Warfarin
- Or NOAC

- No preferences

# Aspirin NICE 2014

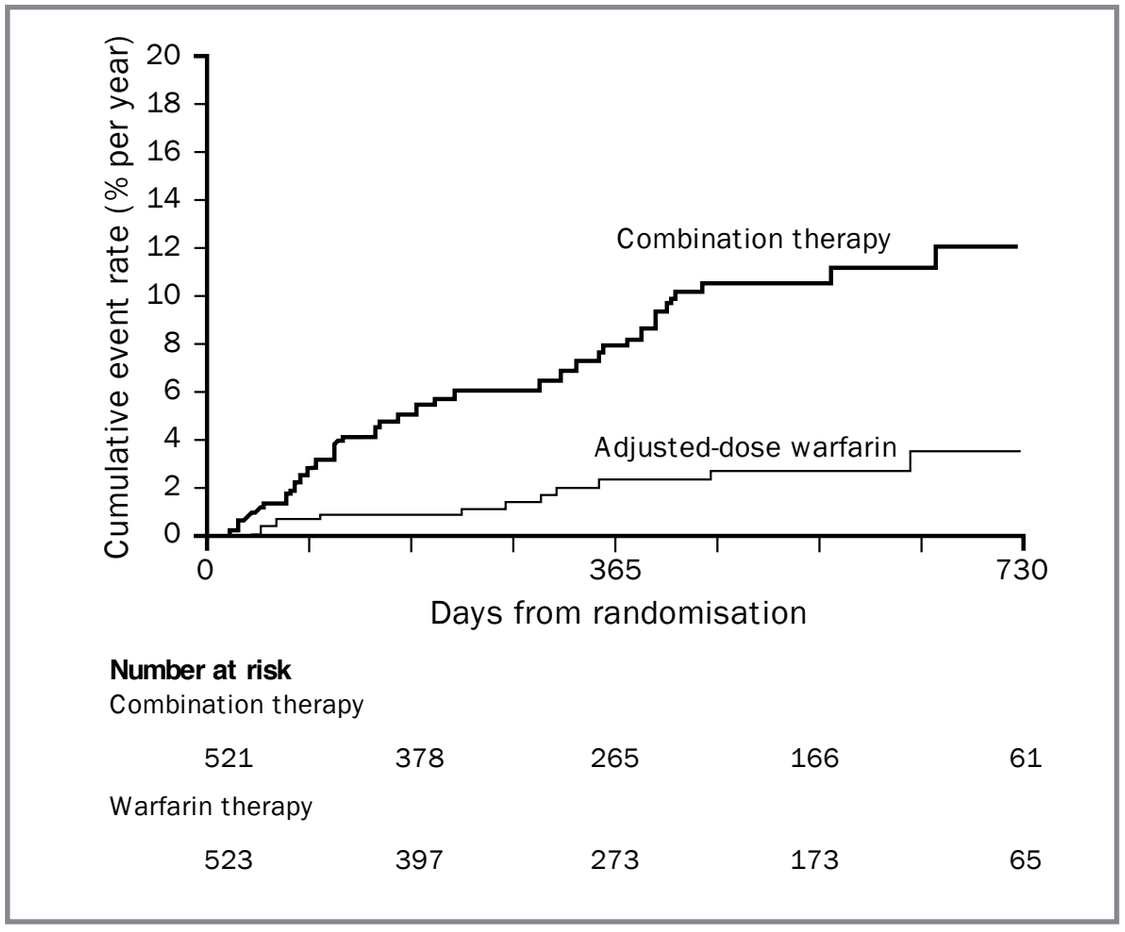
- Do not offer aspirin
- As monotherapy solely for stroke prevention to people with atrial fibrillation

# Aspirin Data

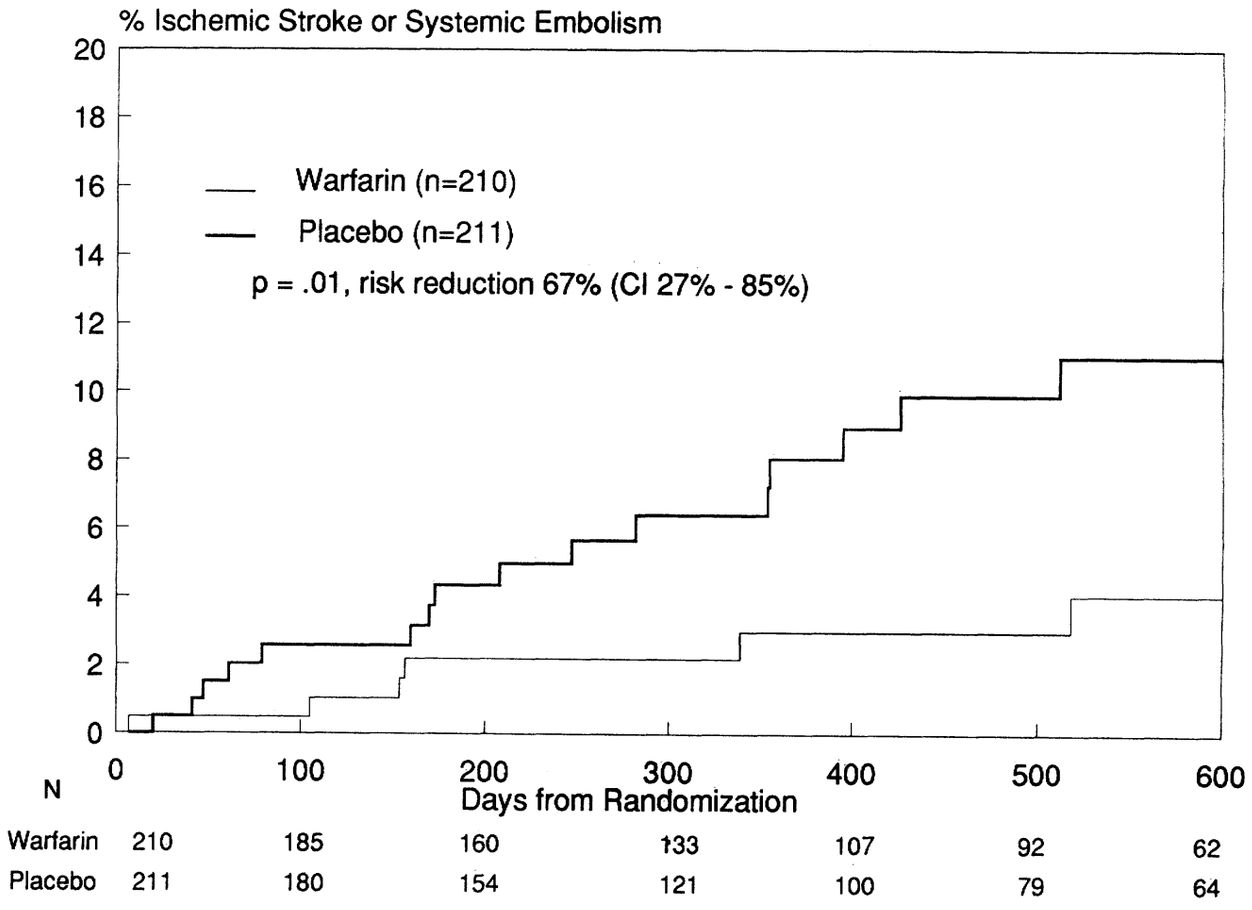



van Walraven et al, JAMA 2002, Oral Anticoagulants vs Aspirin in Nonvalvular Atrial Fibrillation: an Individual Patient Meta-Analysis

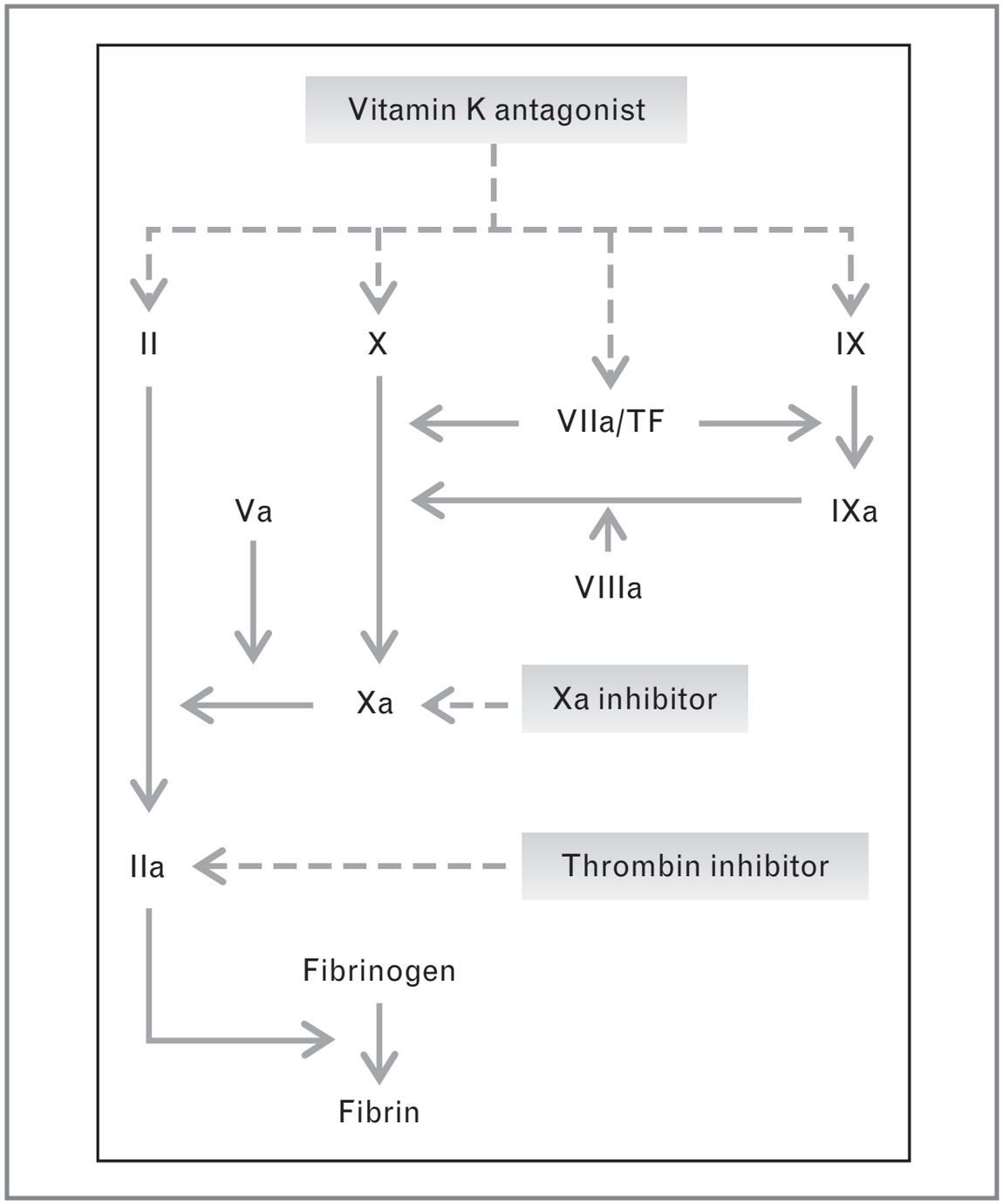
# Warfarin Reduces Stroke Rate




Stroke Prevention in AF Investigators, Lancet 1996

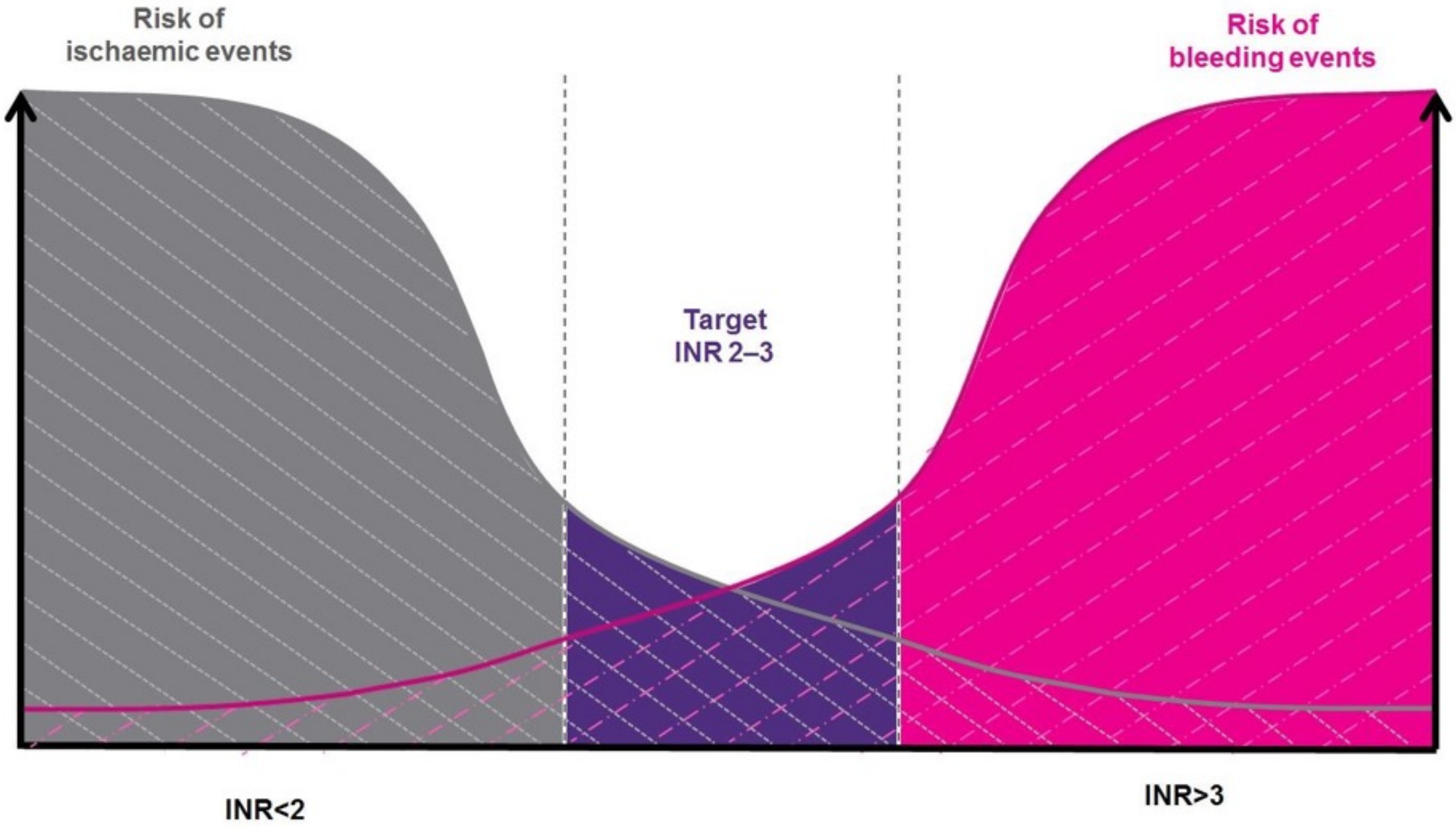



SPAF Study, Circulation 1991




| Potentiate Warfarin | Inhibit Warfarin |
|---|---|
| Acetaminophen | Azathioprine |
| Amiodarone | Carbamazepine |
| Aspirin | Haloperidol |
| Antibiotics (particularly) Cephalosporins, ciprofloxacin, erythromycin metronidazole, trimethoprim-sulfamethoxazole, macrolides | Oral contraceptives |
| Cimetidine | Phenobarbital |
| Excessive ETOH | Rifampin |
| Fluconazole | Vitamin K-containing foods (green leafy vegetables): spinach, broccoli, avocado |
| NSAIDs | Coenzyme Q |
| Sulfonamides | St. John's wort |
| Gingko biloba, ginseng | Hypothyroidism |
| Congestive heart failure | Nephrotic syndrome |
| | Edema |
| | Hereditary coumadin resistance |

# Vitamin K Antagonists (VKAs) have a narrow therapeutic window[6]



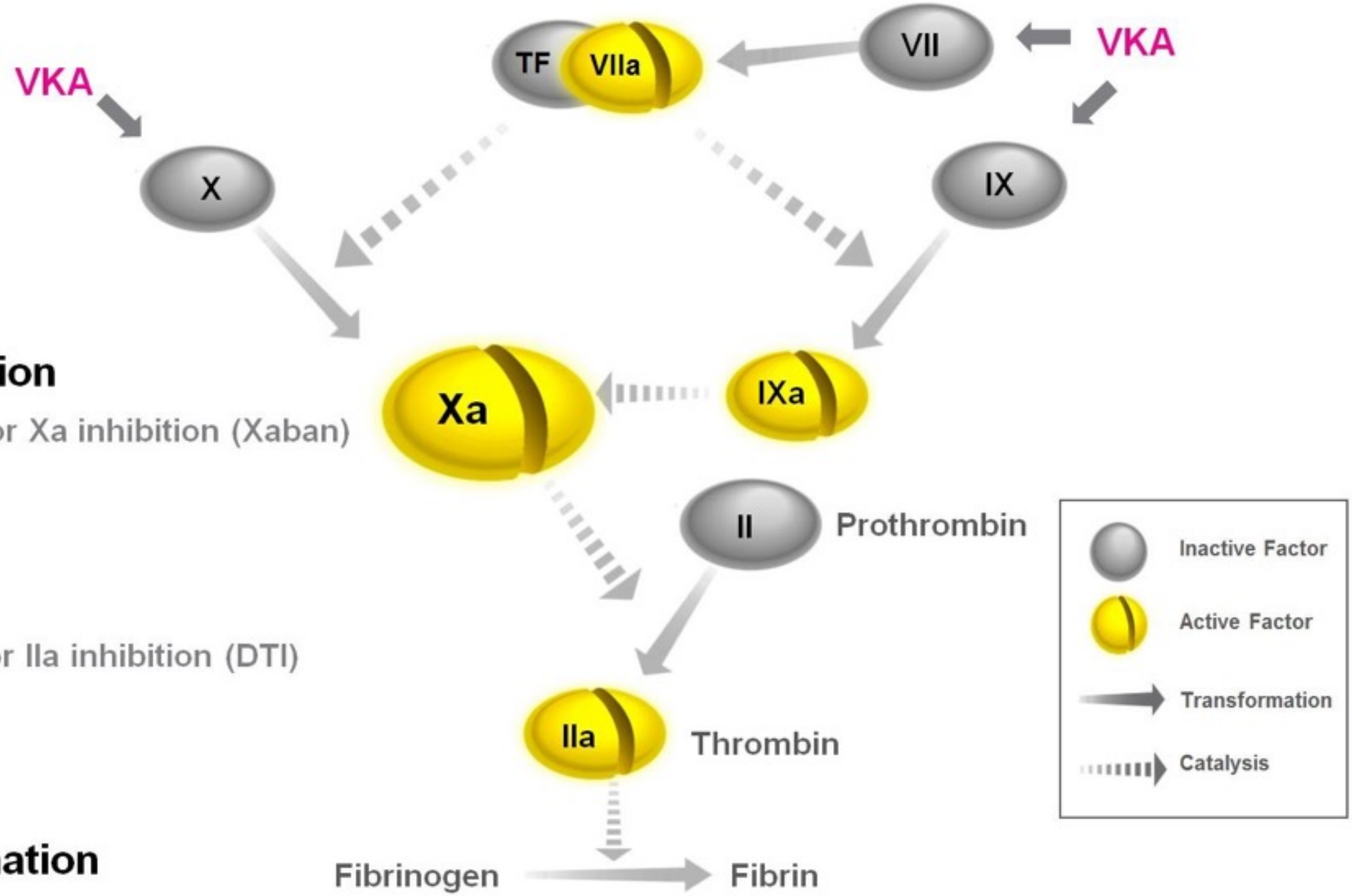



6. Ferreiro JL *et al. Thromb Haemost.* 2010;103(6):1128–1135

# NICE: Labile INRs

- Reassess anticoagulation for a person with poor anticoagulation control shown by any of the following:
  - 2 INR values > 5 or 1 INR value> 8 within the past 6 months
  - 2 INR values less than 1.5 within the past 6 months
  - TTR less than 65%

# Targets for anticoagulants[9,10,11]




Direct Factor Xa inhibition (Xaban)

*apixaban*

*edoxaban*

*rivaroxaban*

Direct Factor IIa inhibition (DTI)

*dabigatran*

## Clot formation

DTI = Direct Thrombin Inhibitor
TF = Tissue factor


9. Piccini JP *et al. Curr Opin Cardiol.* 2010;25(4):312–320;
10. Spyropoulos AC *et al. Expert Opin Investig Drugs.* 2007;16(4):431–440
11. Steffel J and Braunwald *E. Eur Heart J* 2011;doi:10.1093/eurheartj/ehr052

# Xabans and Direct Thrombin Inhibitors (DTIs) have different pharmacological characteristics[12-18]

| | Xabans | | | DTI |
|---|---|---|---|---|
| | rivaroxaban | apixaban | edoxaban | dabigatran |
| Target | Factor Xa | | | Thrombin |
| Prodrug | No | No | No | Yes |
| Oral bioavailability | 80–100%* | ~50% | 60% | 6.5% |
| Renal clearance of absorbed active drug | 33% | 27% | 35% | >80% |
| $T_{max}$ (h) | 2–4 | 3-4 | 1–2 | 2–6# |
| Half-life (h) | 5–13 | 8–13 | 10–14 | 12–14 |
| Fixed Dosing (SPAF indication) | OD | BID | OD | BID |

*15-20mg doses required to be taken with food

#Postoperative period

OD = Once daily
BID = Twice daily

12. Eriksson BI *et al. Annu Rev Med.* 2011;62:41–57
13. Kubitza D *et al. Clin Pharmacol Ther.* 2005;78(4):412–421
14. Lopes RD *et al. Am Heart J.* 2010;159(3):331–339
15. Dabigatran SmPC; 16. Apixaban SmPC; 17. Rivaroxaban SmPC;18. Edoxaban SmPC

# NOACs approved in the EU for stroke prevention in renally impaired patients with NVAF[15-18, 22]

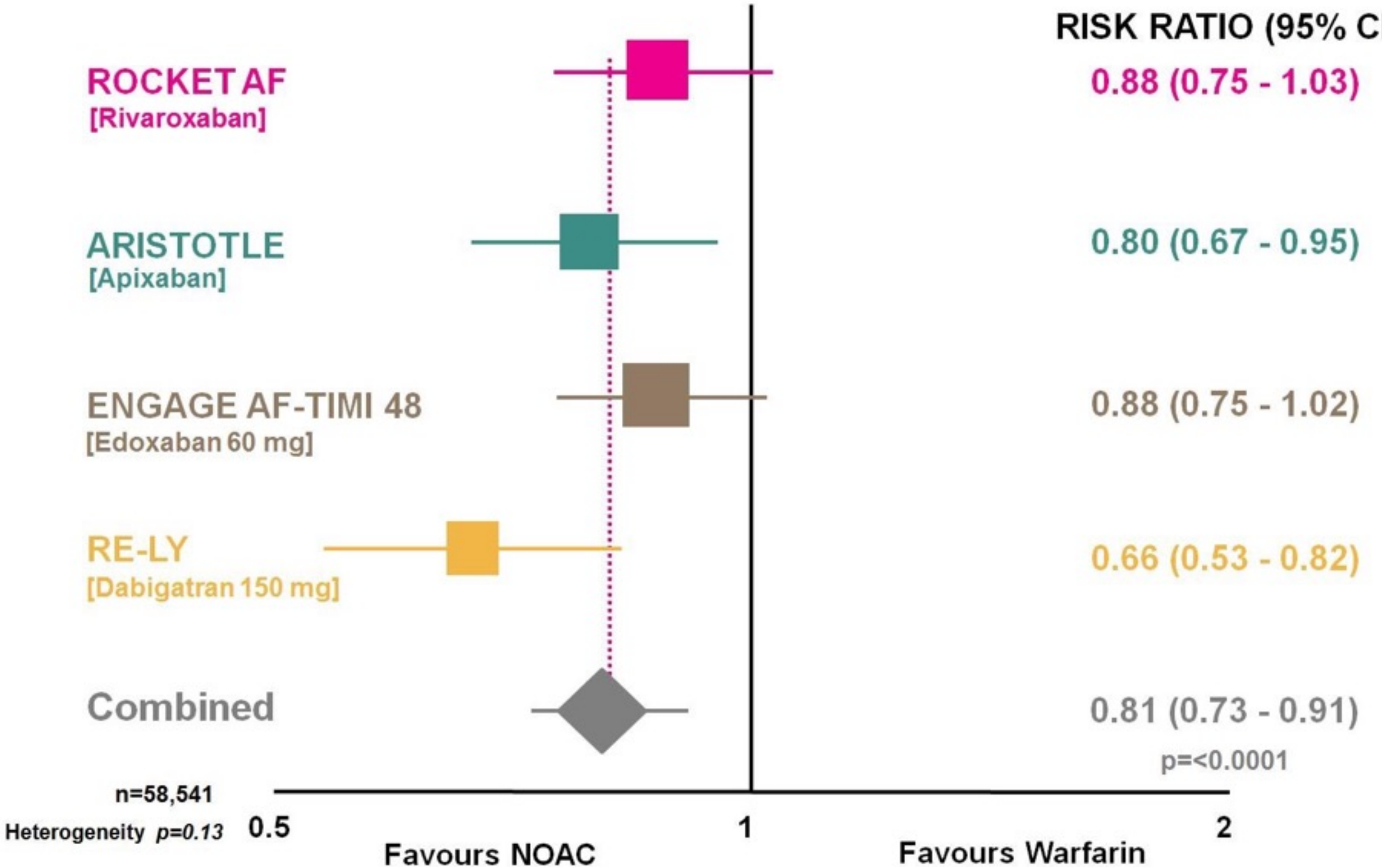
- Rivaroxaban is the only NOAC for which a specific dose was tested prospectively in patients with non-valvular AF (NVAF) and moderate renal impairment[22]

**Dose adjustments for EU-approved NOACs for stroke prevention**

| | rivaroxaban | apixaban | edoxaban | dabigatran |
|---|---|---|---|---|
| Dose | 20 mg OD<br>15 mg OD | 5 mg BID<br>2.5 mg BID | 60 mg OD<br>30 mg OD | 150 mg BID<br>110 mg BID |
| Reduced dose | 15 mg OD if CrCl 30−49 mL/min | 2.5 mg BID if two of the following criteria apply: age ≥80 years, weight ≤60 kg, or creatinine ≥133 µmol/l | 30 mg OD if:<br>CrCl <50 ml/min<br>Weight ≤60 Kg<br>Concomitant use of potent P-gp inhibitors | 110 mg BID if age ≥80 years or age 75−80 years with a risk factor for bleeding |


15. Dabigatran SmPC
16. Apixaban SmPC
17. Rivaroxaban SmPC
18. Edoxaban SmPC
22. Patel MR *et al. N Engl J Med.* 2011;365(10):883–891

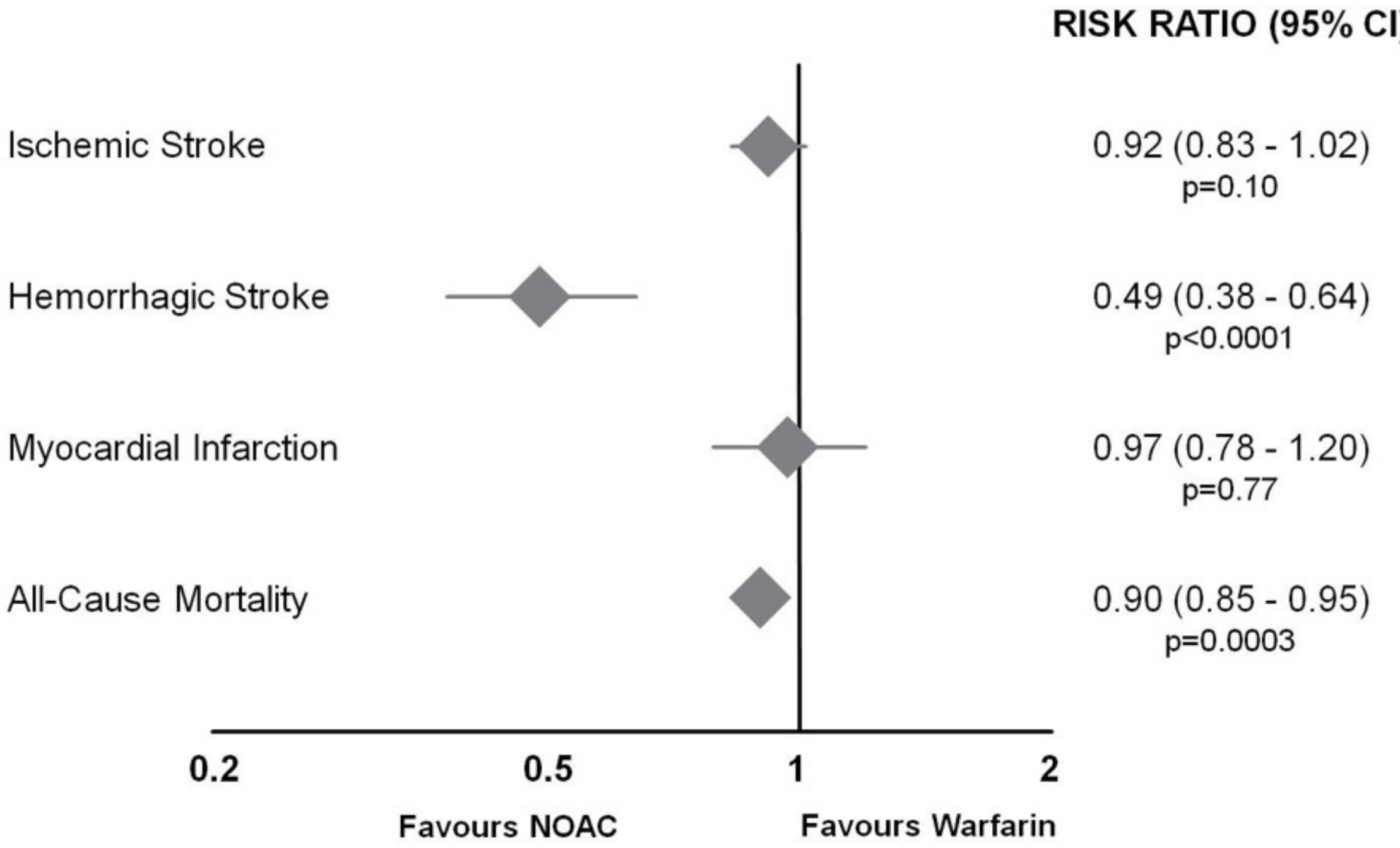
# All NOACs: Stroke or systemic embolism[27]






27. Ruff CT *et al. The Lancet.* 2013. Available at: http://www.pace-cme.org/d/867/meta-analysis-of-large-noac-trials-shows-favourable-risk-benefit-ratio-over-warfarin. Last accessed: February 2016

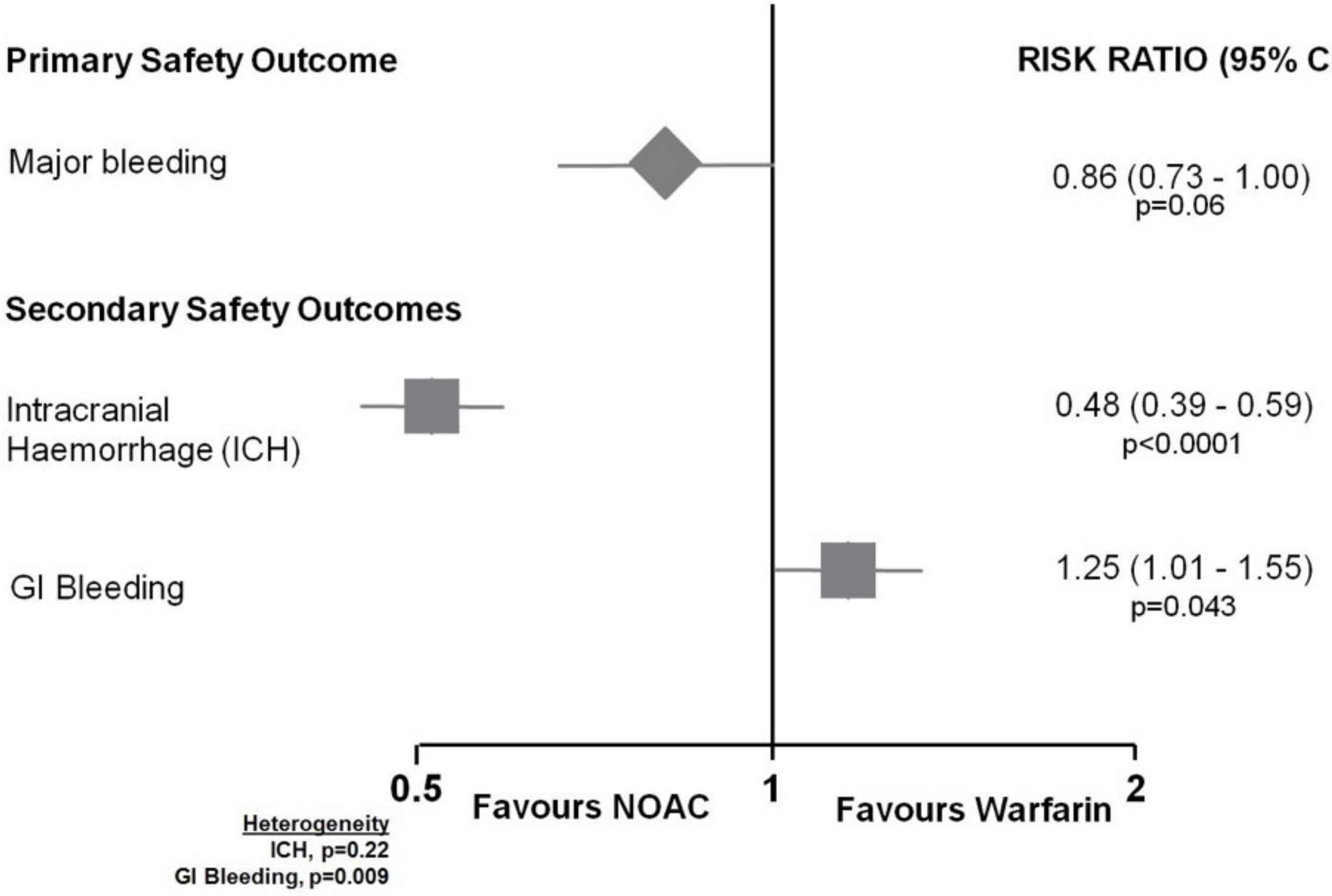
# Secondary efficacy outcomes for all NOACs combined[27]






27. Ruff CT *et al. The Lancet.* 2013. Available at: http://www.pace-cme.org/d/867/meta-analysis-of-large-noac-trials-shows-favourable-risk-benefit-ratio-over-warfarin. Last accessed: February 2016

# Primary and secondary safety outcomes of all NOACs combined[28]






28. Ruff CT *et al. Lancet.* 2014;383(9921):955–962

# Measuring NOAC Anticoagulant Effect

| | Dabigatran | Apixaban | Rivaroxaban |
|---|---|---|---|
| **Plasma peak** | 2h after ingestion | 1-4h post ingestion | 2-4h after ingestion |
| **Plasma trough** | 12-24h after ingestion | 12-24h post ingestion | 16-24h after ingestion |
| **PT** | cannot be used | cannot be used | prolonged: may indicate excess bleeding risk but local calibration required |
| **INR** | **cannot be used** | **cannot be used** | **cannot be used** |
| **aPTT** | at trough >2x ULN suggests excess bleeding risk | cannot be used | cannot be used |
| **dTT** | At trough >200ng/ml ≥ 65s: excess bleeding risk | cannot be used | cannot be used |
| **Anti-FXa assays** | n/a | no data yet | quantitative; no data on threshold values for bleeding or thrombosis |
| **Ecarin clotting time** | at trough >2x ULN: excess bleeding risk | no data yet | not affected |

**Heidbuchel H et al. Europace 2013;15:625-651**

Initiator of anticoagulant treament:

- Sets indication for anticoagulation;
- Makes choice of anticoagulant;
- Decides on need of proton pump inhibitor;
- Baseline haemoglobin, renal and liver function;
- Provides education;
- Hands out anticoagulation card;
- Organizes follow-up (when, by whom, what?);
- Remains responsible coordinator for follow-up.

first FU: 1 month

Follow-up: GP, anticoagulant clinic, initiator of therapy,etc.

- Checks:
  1. Compliance (patient should bring remaining pills);
  2. Thrombo-embolic events;
  3. Bleeding events;
  4. Other side effects;
  5. Co-medications and over-the-counter drugs.
  6. Need for blood sampling?

1 m?
3 m
6 m?

In case of problems: contacts initiator of treatment.

Else: fills out anticoagulation card and sets date/place for next follow-up.

# Blood Sampling

| | |
|---|---|
| Yearly | • Haemoglobin, renal and liver function |
| 6 monthly | • Renal function if CrCl 30–60 ml/min, or if on dabigatran and >75 years or fragile |
| 3 monthly | • If CrCl 15–30 ml/min |
| On indication | • If intercurring condition that may impact renal or hepatic function |

# Dose Changes

| | **Rivaroxaban** | **Apixaban** | **Edoxaban** | **Dabigatran** |
|---|---|---|---|---|
| Usual Dose | 20 mg od | 5 mg bd | 60 mg od | 150 mg bd |
| Reduce dose indications | Reduce if GFR 30-49 ml/min | Reduce if GFR<30 or two or more of: Age≥80yrs Wt ≤60 Kg Creat ≥133 | Reduce if: GFR<50 Wt≤60 Kg Concomitant P-gp inhibitors* | Reduce if: Age≥80 yrs or Age 75-80 with bleeding risks Using verapamil |
| Reduced dose | 15 mg od | 2.5 mb bd | 30 mg bd | 110 mg bd |
| Avoid if: | GFR<15 | GFR<15 | GFR<15 | GFR<30 |

*P-glycoprotein (P-gp) inhibitors: ciclosporin, dronedarone, erythromycin, or ketoconazole.

# Severe NOAC Drug Interactions

- Avoid these drugs
- Increase Levels (up to 150%)
  - Dronedarone
  - Antifungals, e.g., Ketoconazole
  - Protease Inhibitors, e.g., Ritonavir
- Decrease levels (about 50%)
  - Rifampicin
  - St Johns Wort
  - Carbemazepine, Phenytoin, Phenobarbital

# Moderate Drug Interactions with NOACs

- Rivaroxaban should be taken with food (39% variance)
- Quinidine
  - Increase levels by 50%
- Clari/Erythromycin
  - Increase levels 20-50%
- NSAIDs, anti-platelets

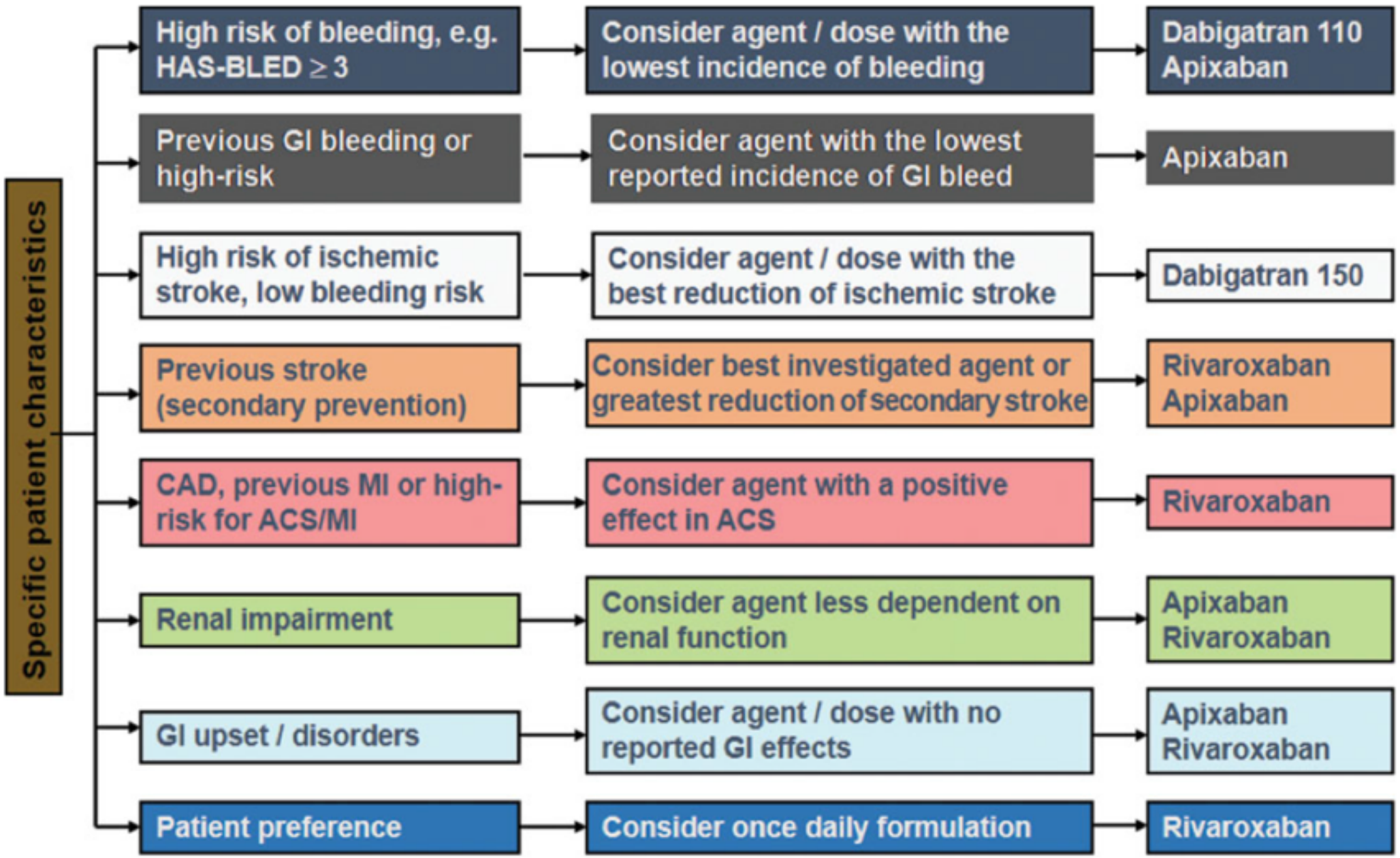
# Switching between Anticoagulants

- NOAC to VKA
  - Continue NOAC until INR>2
  - Measure INR just prior to next dose of VKA
  - Measure INR day after stopping NOAC
- VKA to NOAC
  - Initiated immediately if INR<2
  - If the INR is 2.0–2.5, NOACs can be started immediately or (better) the next day
  - For INR >2.5, repeat INR in 2 days

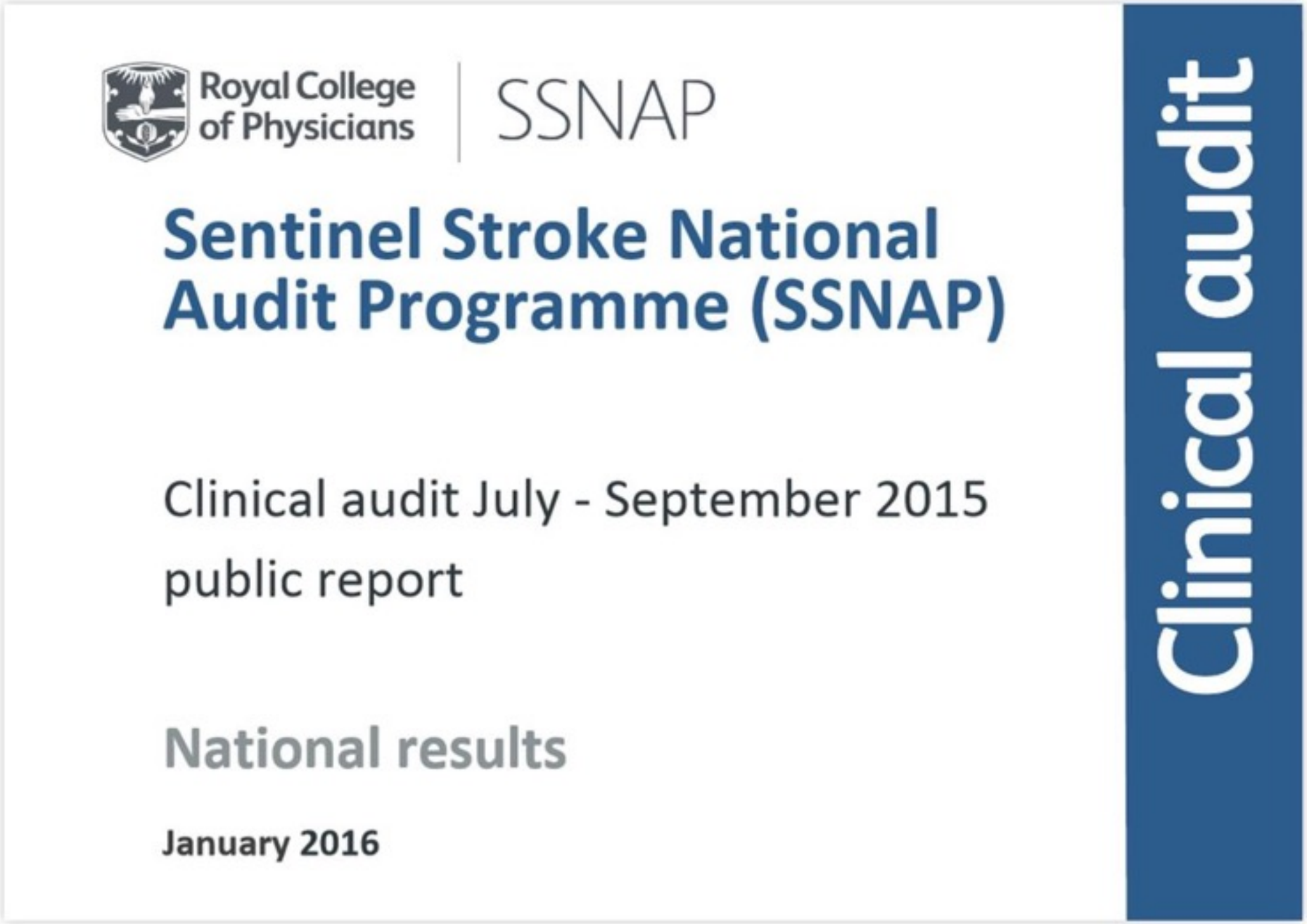
# Dealing with dosing errors

- Missed dose
  - No double dose for missed individual doses
  - Forgotten dose can be taken until half dosing interval elapsed (e.g. up to 12 h for a once daily dosing)
    - If not possible dose skipped & next scheduled dose taken
- Double dose
  - opt to forgo next planned dose
- Overdose, depending on amount of suspected overdose, hospitalisation for monitoring

# Which NOAC?



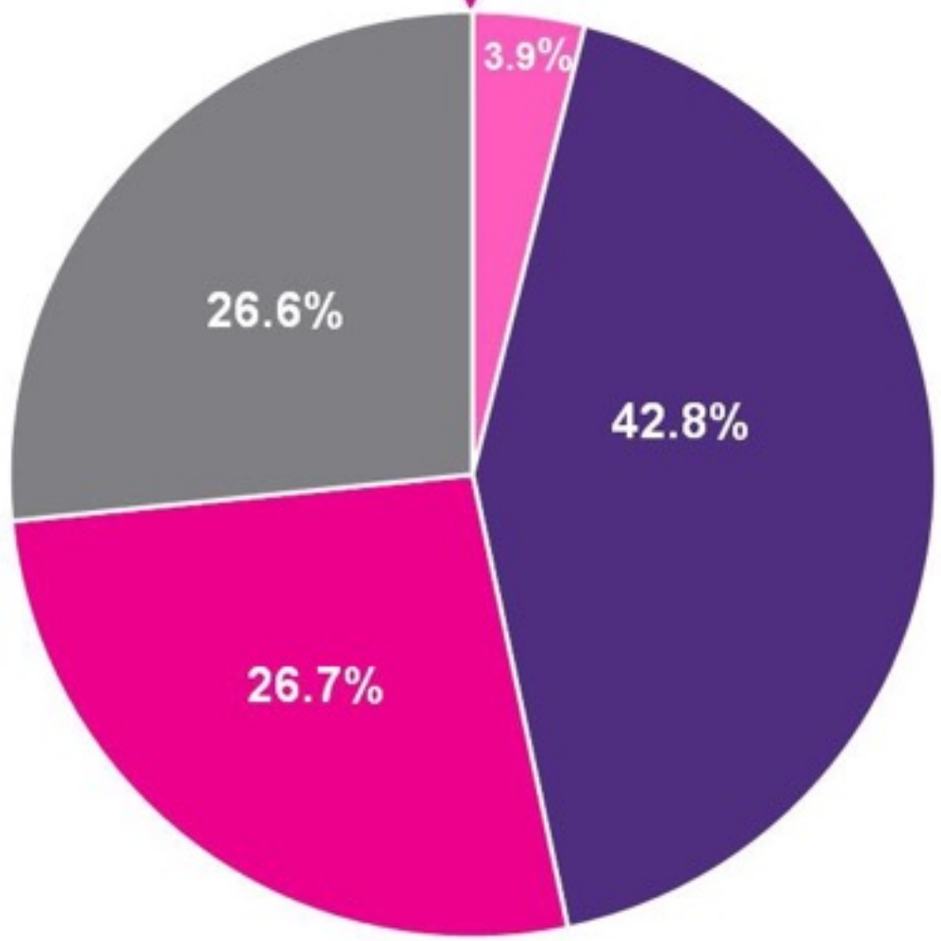

Camm, J. Am J Medicine 2013,; published on line at http://educattion.amjmed.com/00000


Royal College of Physicians
SSNAP
Sentinel Stroke National Audit Programme (SSNAP)
Clinical audit July - September 2015 public report
National results
January 2016
Clinical audit

# …but still less than 50% of AF patients were anticoagulated at time of stroke[23]

July-Sept 2015
England, Wales, Northern Ireland
19,971 stroke admissions

**3,935 in AF (20%)**




Medication prior to admission

- OAC + AP
- OAC only
- AP only
- Neither

OAC = Oral anticoagulant
AP = Antiplatelet



23. SSNAP July-Sept 2015 Public Report, January 2016

Worries over Bleeding?

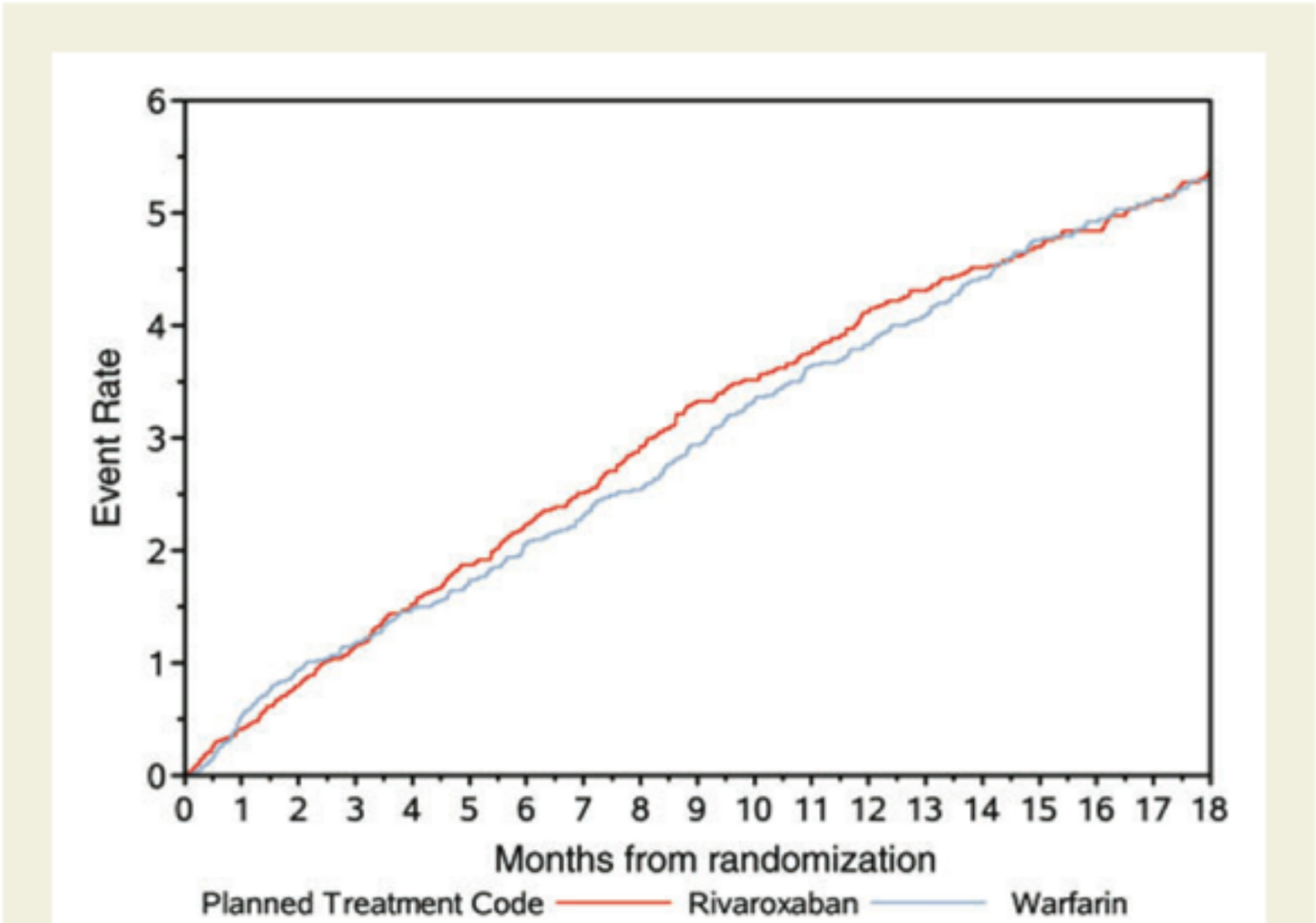
# Patient Attitude To Risk of Anticoagulation

- Patients required 15% relative risk reduction in the risk of stroke to consider anticoagulation
- Patients were willing to endure 4.4 major bleeds in order to prevent one stroke

LaHaye et al, Thromb Haemost. 2014 Mar 3;111(3):465-73

# Bleeding Warfarin vs Rivaroxaban

- No difference in bleeding
- No difference in outcomes




Piccini et al 2014, Euro Heart Journal

# How to manage bleeding complications

**Patient receiving rivaroxaban**

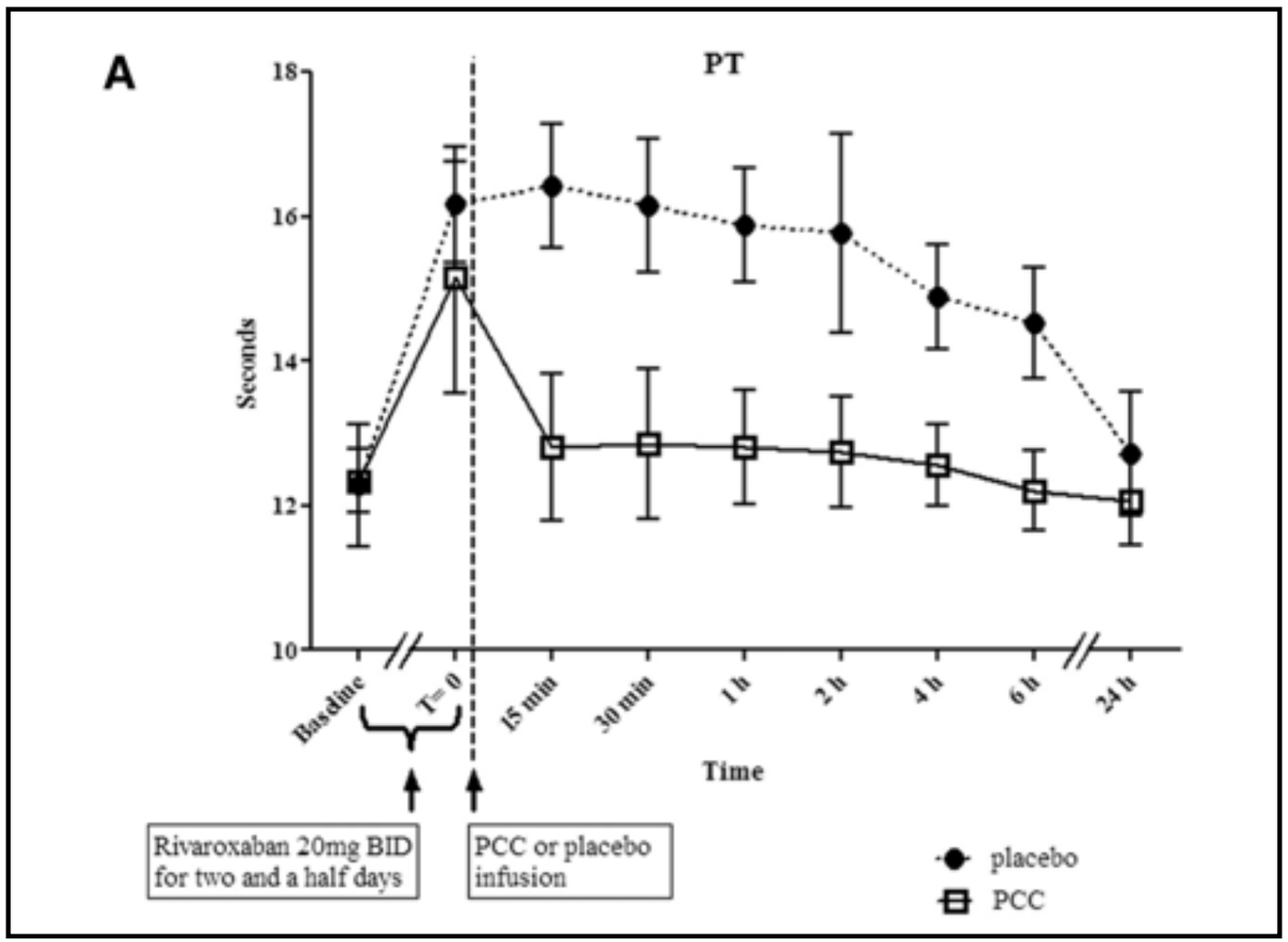
| MILD BLEED | MAJOR BLEED | LIFE THREATENING BLEED |
|---|---|---|
| Delay or discontinue treatment as appropriate<br><br>**Continues to bleed** | Symptomatic treatment such as:<br>◆ Mechanical compression<br>◆ Surgical / radiological intervention<br>◆ Fluid replacement<br>◆ Haemodynamic support<br>◆ Blood product or component transfusion | Seek specialist Haemostasis/ Haematology advice. Consider administration of specific procoagulant reversal agent should be considered, such as:<br>◆ prothrombin complex concentrate (PCC)<br>◆ activated prothrombin complex concentrate (APCC) or<br>◆ recombinant factor VIIa (r-VIIa)<br>However there is limited clinical experience with the use of these products receiving rivaroxaban. Due to the high plasma protein binding, rivaroxaban is not expected to be dialyzable |


UKXAR06160140
July 2016

11. Rivaroxaban SmPC https://www.medicines.org.uk/emc/medicine/25591

# Dealing with bleeding - Rivaroxaban

- Prothrombin complex concentrate
- Immediately & completely reverses the anticoagulant effect of rivaroxaban




Circulation. 2011;124:1573-1579.

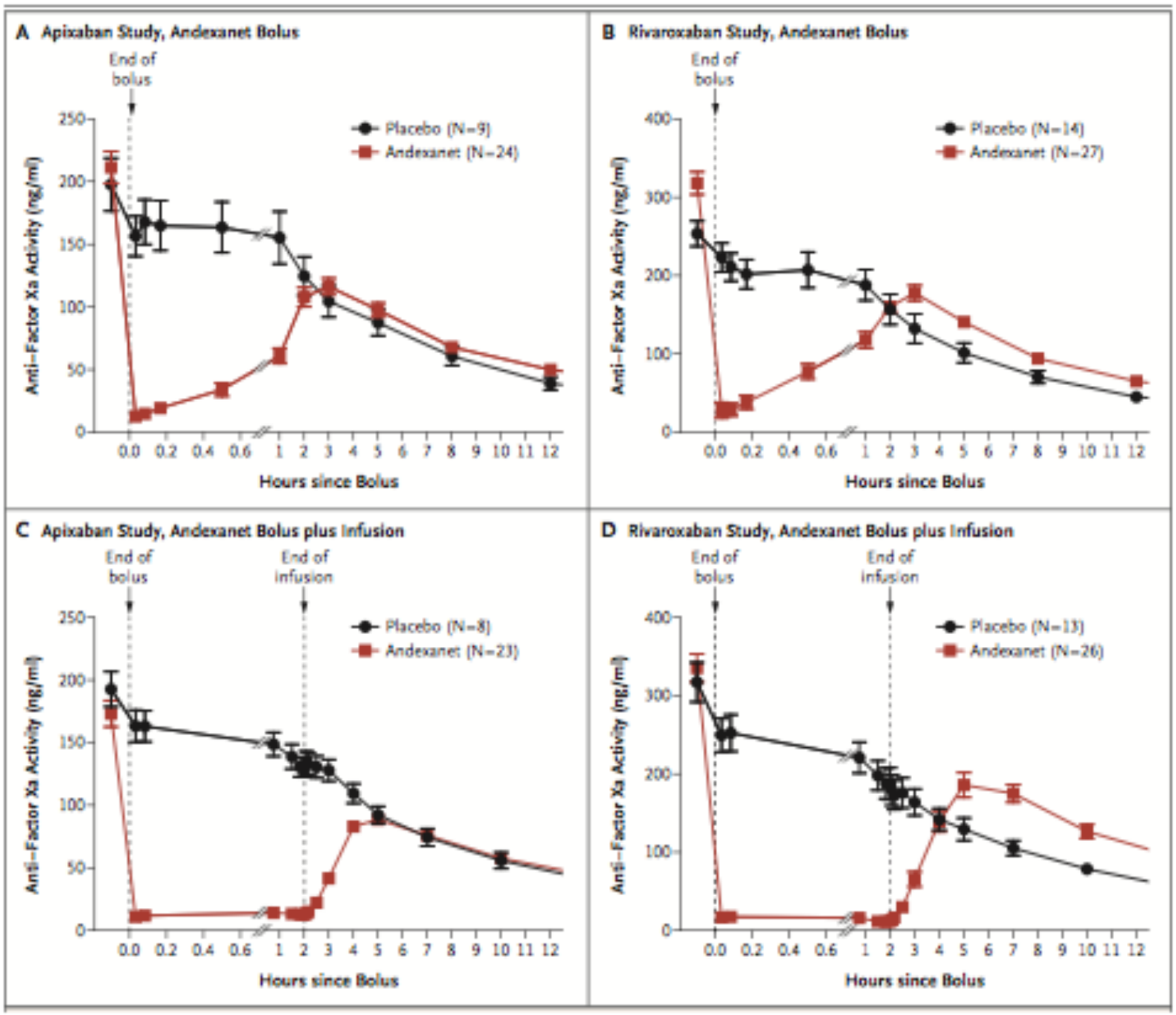
# Andexanet alfa (andexanet)*

- Specific reversal agent
- Recombinant modified human factor Xa decoy protein
- Neutralize both direct and indirect factor Xa inhibitors
- Rapidly reversed apixaban-induced and rivaroxaban-induced changes
- In anti–factor Xa activity and thrombin generation without serious adverse events

*Currently Unlicenced

Siegal et al. NEJM 2015

# Andexanet

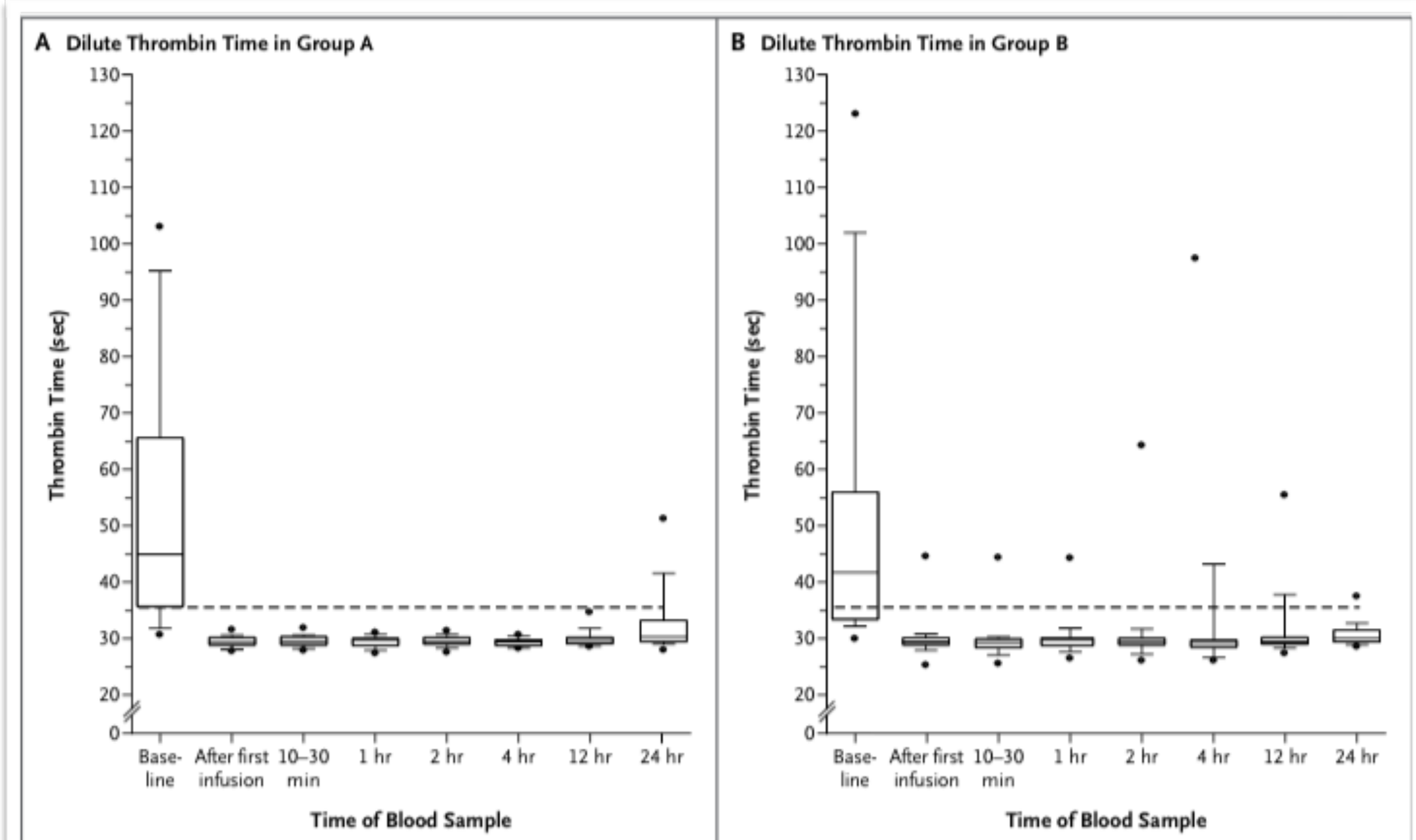

A Apixaban Study, Andexanet Bolus
End of bolus
Placebo (N=9)
Andexanet (N=24)
Anti–Factor Xa Activity (ng/ml)
Hours since Bolus
B Rivaroxaban Study, Andexanet Bolus
End of bolus
Placebo (N=14)
Andexanet (N=27)
Anti–Factor Xa Activity (ng/ml)
Hours since Bolus
C Apixaban Study, Andexanet Bolus plus Infusion
End of bolus
End of infusion
Placebo (N=8)
Andexanet (N=23)
Anti–Factor Xa Activity (ng/ml)
Hours since Bolus
D Rivaroxaban Study, Andexanet Bolus plus Infusion
End of bolus
End of infusion
Placebo (N=13)
Andexanet (N=26)
Anti–Factor Xa Activity (ng/ml)
Hours since Bolus

# Idarucizumab for Dabigatran Reversal

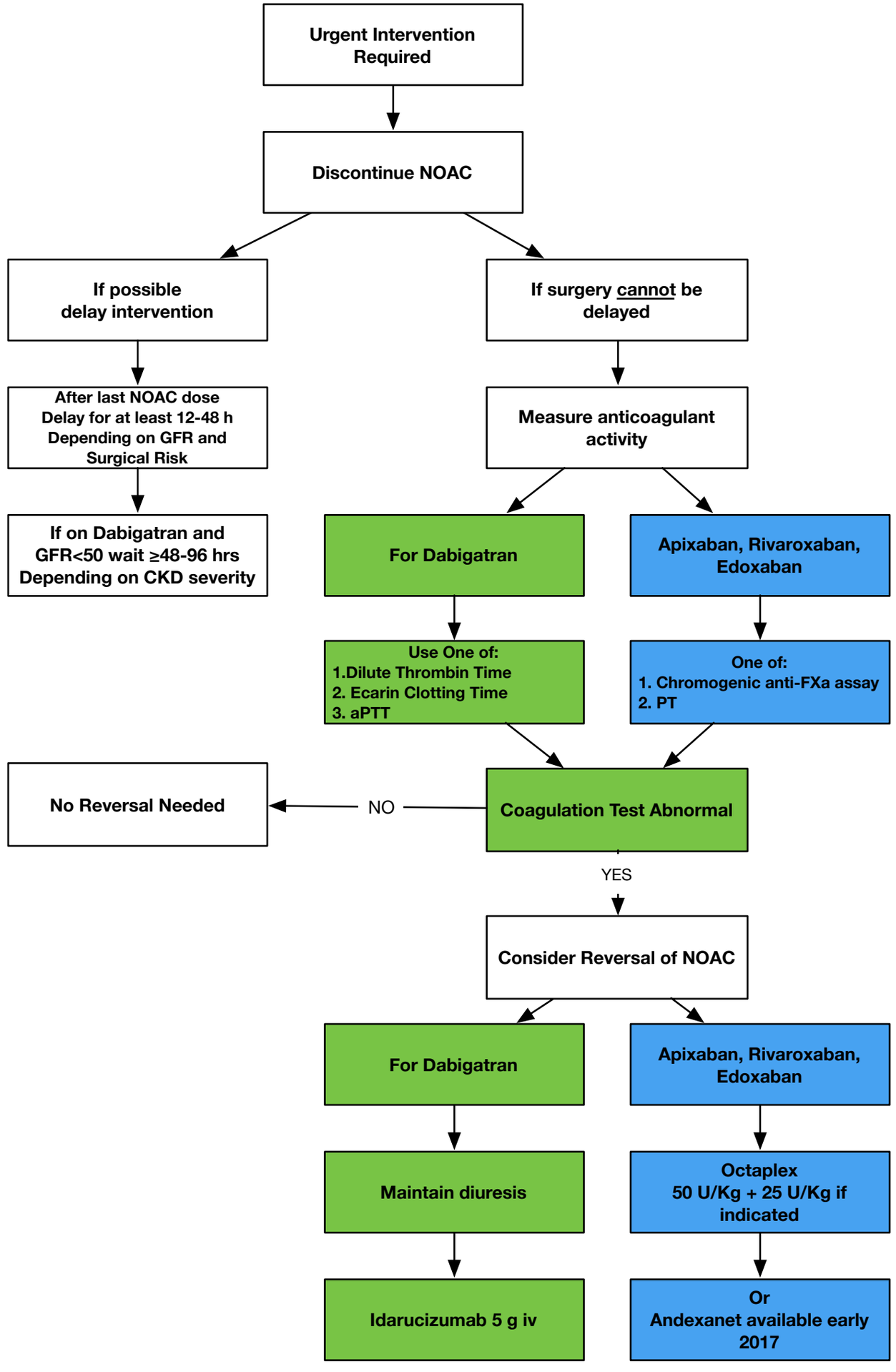
- Monoclonal antibody fragment
- Reverse Dabigatran in serious bleeding or needing urgent procedure
- Complete reversal within minutes
- Dilute thrombin time was normalised in 98% of patients in grp A, 93% in grp B

Pollack et al NEJM 373:511-520 (2015)

# Idarucizumab for Dabigatran Reversal



# Urgent Surgery



# Elective Surgery Decision to Bridge

Is it considered safe to do the procedure with the patient on warfarin?

Yes → Continue. Check INR is within required limits

No

Stop warfarin 5 days before procedure

Is the patient at high risk from withdrawal of anticoagulation

Yes

Confirm no allergy to heparin

Check FBC, U+Es, LFTs and INR and make a note that you have checked it on the relevant pre-op document

Check eGFR >30 and platelets >100xd$10^9$/l

**Dalteparin bridging**

No → All other patients are at low risk from withdrawal of anticoagulation. Low risk patients do not need prophylactic Dalteparin pre-procedure. Assess patient for risk of VTE and prescribe post-procedure prophylactic dalteparin accordingly.

No? discuss with anaesthetist or haematologist

**Patients at high risk from withdrawal of anticoagulation**

**Heart valve**

- Rheumatic valvular heart disease
- Mechanical mitral valve
- Mechanical aortic valve (including bileaflet) with one of the following risk factors: AF, prior stroke/TIA, hypertension, diabetes, heart failure, age >75 years)

**AF**

- No bridging. Discuss patient with anaesthetist if CHADS2 score 6 or Stroke or TIA within 3 months. NEJM Perioperative Bridging Anticoagulation in Patients with AF, Douketis, et al. June 2015

To calculate the $CHADS_2$ score (score 1 for each of the following)

- **C**CF
- **H**ypertension
- **A**ge >75
- **D**iabetes
- Previous **S**troke or TIA (scores 2)

**VTE**

Recurrent VTE

Single VTE & severe thrombophilia (antithrombin deficiency, antiphospholipid syndrome)

**NB:** if DVT <3 months defer surgery or consider IVC filter if this is not possible

**Stroke/embolism**

Recurrent stroke or embolism

Stroke/TIA <3 months

**Cardiac failure**

With cardiac aneurysm

+/- thrombus

| Actual body weight Kg | Dalteparin dose (units) |
|---|---|
| Under 46 | 7500 once daily |
| 46 – 56 | 10000 once daily |
| 57 – 68 | 12500 once daily |
| 69 – 82 | 15000 once daily |
| 83 and over | 18000 once daily |
| >110 Kg | You may wish to discuss giving a higher dose although this is unlicensed. |

**Pre-procedure**

- Check patient's INR record when you photocopy it.
  - If the control is good, stop 5 days pre-procedure
  - If INR >4 consider stopping warfarin earlier
- Start therapeutic Dalteparin 3/7 pre-procedure
- Give further therapeutic Dalteparin 2/7 pre-procedure.
- Give prophylactic dose Dalteparin in the evening before surgery.
- Fill out clotting screen request form for the day of surgery and file in the healthcare record.

*See page 3 for day of procedure guidance*

# NOAC Drug Cessation Prior To Surgery

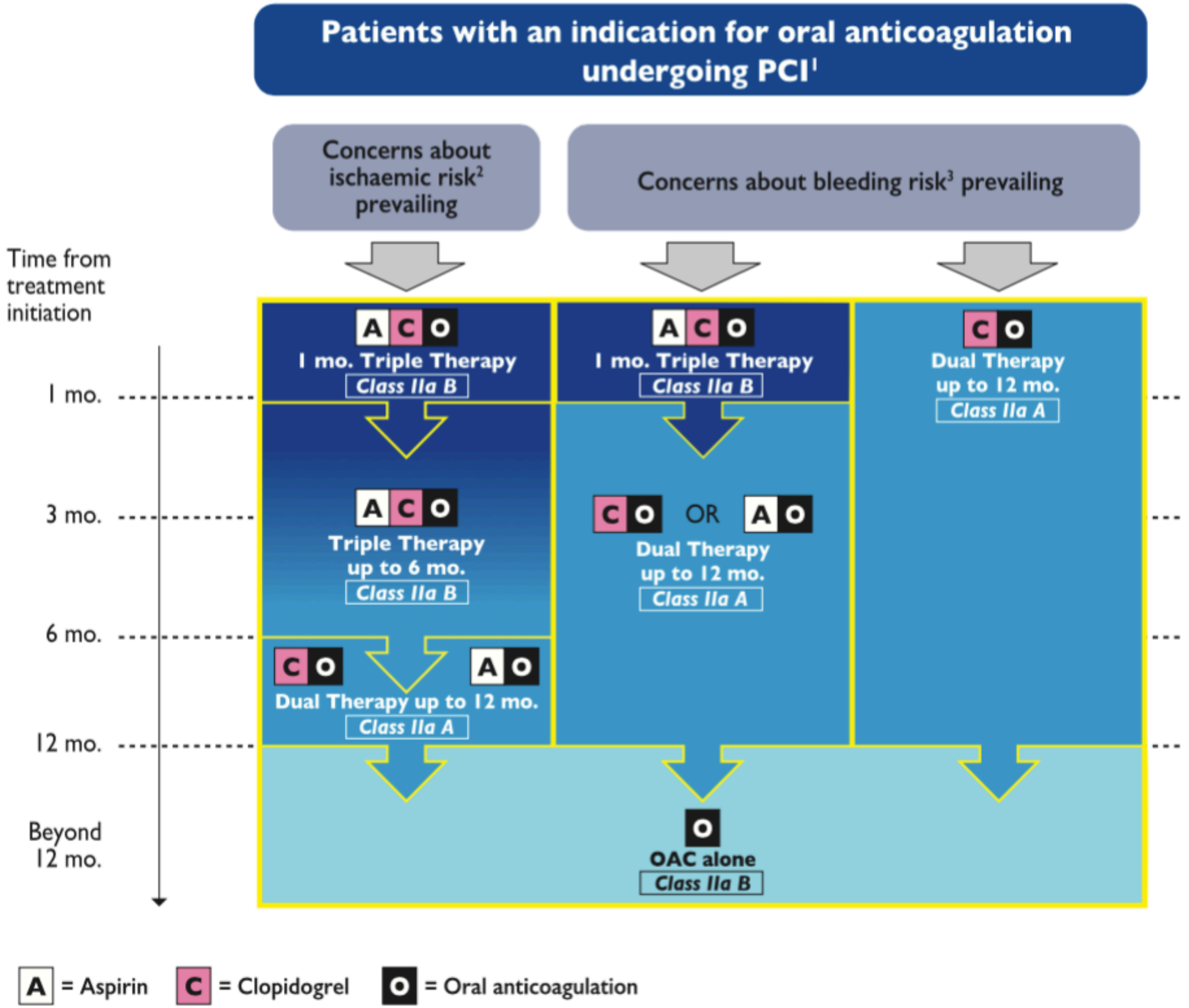
| | **Last intake of drug before elective surgical intervention** | | | |
|---|---|---|---|---|
| | No important bleeding risk and/or adequate local haemostasis possible: perform at trough level (i.e. ≥ 12 or 24 h after last dose) | | | |
| | Dabigatran | | Apixaban, Edoxaban, Rivaroxaban | |
| | Low risk | High risk | Low risk | High risk |
| GFR ≥ 80 | ≥24 h | ≥48 h | ≥24 h | ≥48 h |
| GFR 50-80 | ≥36 h | ≥72 h | ≥24 h | ≥48 h |
| GFR 30-50 | > 48 h | ≥96 h | ≥24 h | ≥48 h |
| GFR 15-30 | Not indicated | Not indicated | ≥36 h | ≥48 h |
| GFR<15 | No official indication for use | | | |
| There is no need for bridging with LMWH/UFH | | | | |

Low risk: with a low frequency of bleeding and/or minor impact of a bleeding; high risk with a high frequency of bleeding and/or important clincial impact. See also Table ****.

Thank you

Questions?

# Extra Slides




See next slide for ischaemia vs bleeding risk factors

# Balancing Risks IHD vs Bleeding on OAC and antiplatelets

**Table 5 High-risk features of stent-driven recurrent ischaemic events**

| |
|---|
| • Prior stent thrombosis on adequate antiplatelet therapy |
| • Stenting of the last remaining patent coronary artery |
| • Diffuse multivessel disease especially in diabetic patients |
| • Chronic kidney disease (i.e. creatinine clearance <60 mL/min) |
| • At least three stents implanted |
| • At least three lesions treated |
| • Bifurcation with two stents implanted |
| • Total stent length >60 mm |
| • Treatment of a chronic total occlusion |



**Table 6 Unfavourable patient profile for a combination of oral anticoagulant and antiplatelet therapy**

| |
|---|
| • Short life expectancy |
| • Ongoing malignancy |
| • Poor expected adherence |
| • Poor mental status |
| • End stage renal failure |
| • Advanced age |
| • Prior major bleeding/prior haemorrhagic stroke |
| • Chronic alcohol abuse |
| • Anaemia |
| • Clinically significant bleeding on dual antithrombotic therapy |

**Patient with AF suffering from an intracranial bleed on OAC**
**If acute event: establish intensity of anticoagulation (see bleeding flow chart)**

**Contra-indication for OAC**

**Consider further information to allow informed judgement**

**Factors supporting withholding of OAC:**

Bleeding occured on adequately dosed NOAC or in setting of treatment interruption or underdosing
Older age
Uncontrolled hypertension
Cortical bleed
Severe intracranial bleed
Multiple microbleeds (e.g. >10)
Cause of bleed cannot be removed or treated
Chronic alcohol abuse
Need for dual antiplatelet therapy after PCI

**Factors supporting reinitiation of OAC:**

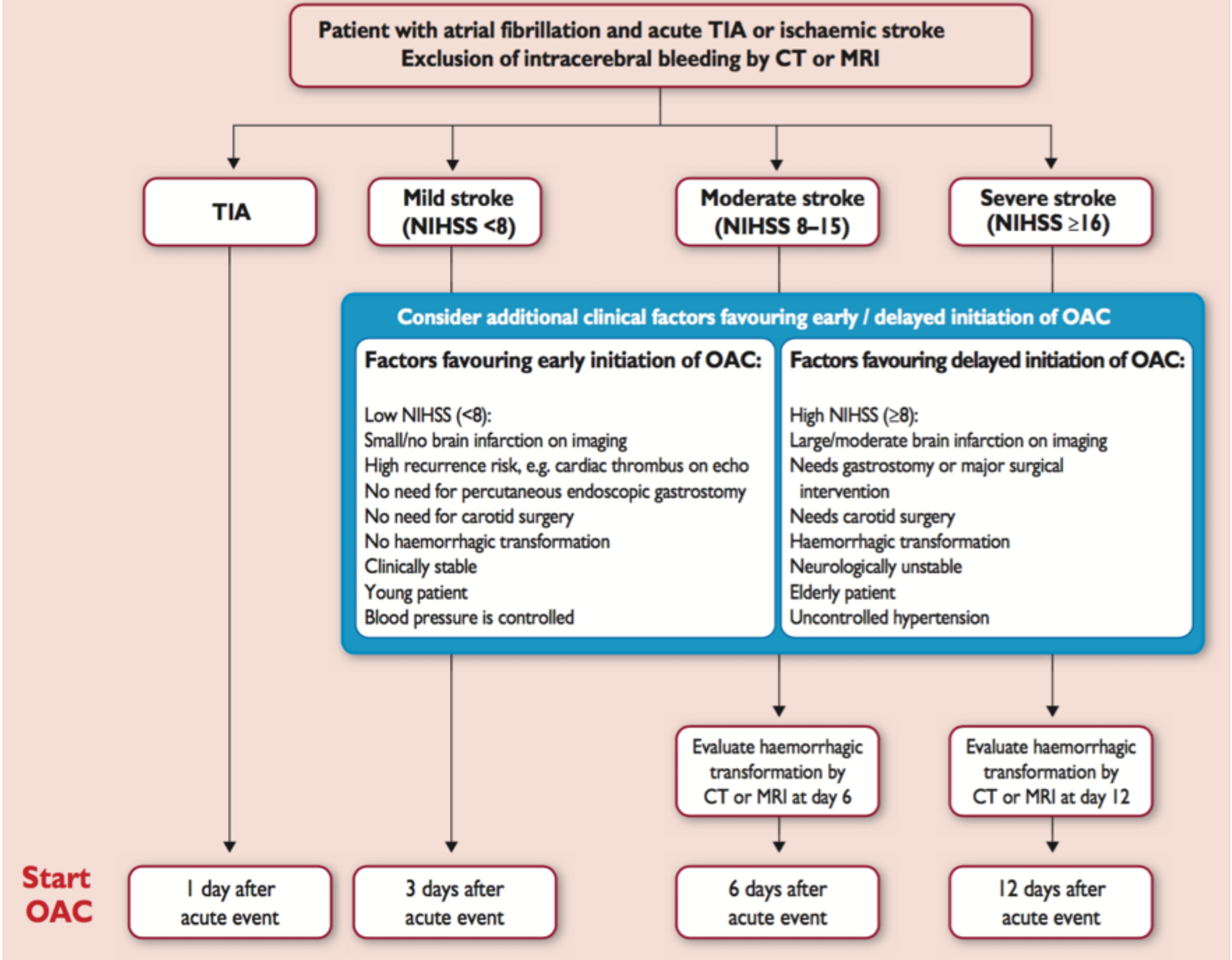
Bleeding occured on VKA or in setting of overdose
Traumatic or treatable cause
Younger age
Well controlled hypertension
Basal ganglia bleed
No or mild white matter lesions
Surgical removal of subdural haematoma
Subarachnoid bleed: aneurysm clipped or coiled
High-risk of ischaemic stroke

**Patient or next of kin choice informed by multidisciplinary team advice**

**No stroke protection (no evidence)**

**LAA occlusion (IIbC)**

**Initiate or resume OAC, choosing an agent with low intracranial bleeding risk, after 4–8 weeks (IIbB)**


Patient with atrial fibrillation and acute TIA or ischaemic stroke
Exclusion of intracerebral bleeding by CT or MRI
TIA
Mild stroke (NIHSS <8)
Moderate stroke (NIHSS 8–15)
Severe stroke (NIHSS ≥16)
Consider additional clinical factors favouring early / delayed initiation of OAC
Factors favouring early initiation of OAC:
Low NIHSS (<8):
Small/no brain infarction on imaging
High recurrence risk, e.g. cardiac thrombus on echo
No need for percutaneous endoscopic gastrostomy
No need for carotid surgery
No haemorrhagic transformation
Clinically stable
Young patient
Blood pressure is controlled
Factors favouring delayed initiation of OAC:
High NIHSS (≥8):
Large/moderate brain infarction on imaging
Needs gastrostomy or major surgical intervention
Needs carotid surgery
Haemorrhagic transformation
Neurologically unstable
Elderly patient
Uncontrolled hypertension
Evaluate haemorrhagic transformation by CT or MRI at day 6
Evaluate haemorrhagic transformation by CT or MRI at day 12
Start OAC
1 day after acute event
3 days after acute event
6 days after acute event
12 days after acute event